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THE ACTIVITY AND STABILITY OF TERTIARY AMINE CATALYSTS IN THE PRESENCE OF HYPOCHLOROUS ACID

Master´s Programme in Chemical, Biochemical and Materials Engineering
Major in Biomass Refining

Master's thesis for the degree of Master of Science in Technology
Submitted for inspection, Espoo, 31st July, 2018

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Abstract of master's thesis

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Major Biomass Refining

Thesis supervisor Professor Tapani Vuorinen

Thesis advisor(s) / Thesis examiner(s) Dr Jordan Perrin

Date	Number of pages	Langauge
31.07.2018	63(+13)	English

Abstract

Hypochlorous acid is an electrophilic oxidizing agent capable of reacting with a range of unsaturated organic substrates. Previously, these reactions have been shown to be catalysed by the use of a tertiary amine, and H_{cat} hardwood pulp bleaching stages using the tertiary amine DABCO, as well as its derivative CM-DABCO, have proved efficient. Within this work, a range of DABCO-derivative structures were synthesised, and their catalytic abilities and stabilities were tested via the use of stopped-flow UV-Vis spectroscopy.

DABCO-derivatives produced in this work all involved mono-N-substitution, and generally high yields could be achieved in simple synthetic routes. Derivative structures tested included allyl (AL), carboxymethyl (CM), carboethoxymethyl (CEM), carbamoylmethyl (AA) and 2-hydroxyethyl (EA) groups. The pKa of the tertiary amine group within these were measured, and found to each be between 3.0 and 3.4, close to the second pKa of DABCO itself (2.97).

Both pH and substrate structure were found to have a significant impact on the catalytic ability of all the tested structures. Due to the chlorinating action of Cl_2 at pH 3, and the large difference between pH and DABCO-derivative catalyst pKa at pH 7, generally low catalytic factors were found at these pH values. At pH 5, higher catalytic factors could be found, with a catalyst pKa closer to 5 producing an increased catalytic ability. The substrate structure affects the rates of catalysis but not the order of activities between the different catalysts. CM-DABCO was the most active derivative for all substrates at pH 5, and it was concluded that further increases to the catalyst pKa could further improve the results obtained.

Unlike DABCO, all the synthesised derivatives were shown to be close to fully stable for up to 10 seconds of pre-incubation with hypochlorous acid. Stability is concluded then to not be a concern in the selection and design of an optimal DABCO-derivative catalyst structure.

Keywords Tertiary amine, Catalysis, Hypochlorous acid, DABCO, Stopped-flow, UV-Vis spectroscopy

Preface

Thank you first of all to the sponsors of the catalytic bleaching project; Andritz Oy, Fibria Celulose, Kemira Oyj, Metsä Group, Stora Enso Oyj, UPM-Kymmene Oyj and Aalto University for the financing of this thesis and the helpful advice during meetings.

A huge thank you also to Professor Tapani Vuorinen, for accepting me into this project and for his guidance throughout, and to Dr Jordan Perrin, who has been a constant source of instruction, useful advice and fun conversations.

In addition, thank you to Markus Kyllönen for performing the pKa titrations of the catalysts that were vital towards my results analysis.

Thanks to all of my family, and to my friends within Puunjalostajakilta and elsewhere who have provided support, chats and coffee drinking company throughout the whole thesis process. Particular thanks to Karl Mihhels, who has been always willing to chat, no matter the time or the circumstances.

Finally, a special thank you to Lumi Ketola, who has been with me through both the good times and the bad, and has made both of them better.

Espoo, 31st July 2018.

Owain George John Dawson

Abbreviations

AA-DABCO	1-carbamoylmethyl-1-azonia-4-aza-bicyclo[2.2.2]octane chloride
AL-DABCO	1-allyl-1-azonia-4-aza-bicyclo[2.2.2]octane chloride
CM-DABCO	1-carboxymethyl-1-azonia-4-aza-bicyclo[2.2.2]octane chloride
CEM-DABCO	1-carboethoxymethyl-1-azonia-4-aza-bicyclo[2.2.2]octane chloride
DABCO	1,4-diazabicyclo[2,2,2]octane / Triethylenediamine
D_{cat}	Catalytic chlorine dioxide bleaching
EA-DABCO	1-(2-hydroxyethyl)-1-azonia-4-aza-bicyclo[2.2.2]octane chloride
HexA	Hexenuronic Acid
H_{cat}	Catalytic hypochlorous acid bleaching
NMR	Nuclear Magnetic Resonance
UV-Vis	Ultraviolet-visible light

Contents

Introduction

Improving the economic and environmental aspects of chemical processes is of vital importance within the world today. Oxidation is a crucial chemical reaction that occurs throughout nature, as well as within human applications across a range of industries. As such, there are many oxidizing agents currently utilised.

Sodium hypochlorite (NaOCl) is a commonly used oxidizing agent, capable of forming different free chlorine species including hypochlorous acid (HOCl), hypochlorite ions ($^{-}$OCl) and chlorine (Cl_2) within aqueous solutions[1,2]. It is particularly important for two uses; in household and commercial disinfection[3], and within chemical synthesis[4–6], but has also in past times been utilised within wood pulp bleaching[7]. Hypochlorous acid also has relevance within water treatment, where it is generally assumed to be the active species of the chlorination disinfection steps[8], and is also generated in mammalian cells to kill harmful pathogens[9].

Within chemical synthesis, sodium hypochlorite is both a key oxidation, as well as chlorination, reagent, and is used in the production of chlorohydrins from alkenes[5]. It can also oxidize alkenes to epoxides[6,10–12], as well as primary and secondary alcohols to aldehydes, carboxylic acids and ketones, especially via the additional use of TEMPO[13,14]. The TEMPO-NaOCl combination is also featured in nanocellulose production via cellulose oxidation[15].

One possibility to increase the rate, and hence feasibility, of many reactions featuring HOCl is via the use of tertiary amine catalysts.[16] The reaction between HOCl and a tertiary amine rapidly forms a chlorammonium cation (R_3N^+-Cl), as shown in Figure 1, which is a stronger electrophile than HOCl itself. Hence, the rate of reaction with nucleophilic unsaturated groups is greatly increased.

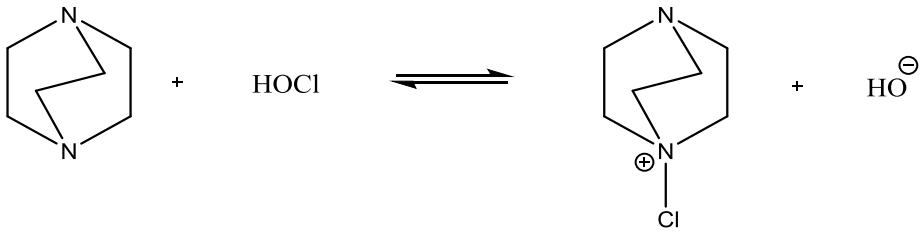


Figure 1: The reaction between DABCO and HOCl to generate the chlorammonium cation.

Many different tertiary amines have been shown to participate in this catalytic process. This includes DABCO[17–19], as well as quinine, quinuclidine and trimethylamine[16,20], amongst others. A main conclusion drawn is that the ability to catalyse depends heavily on the tertiary amine structure, with different structures having an impact on both their activities and stabilities in the HOCl reaction medium[16,20-21].

DABCO (Figure 2) is a commonly used industrial catalyst for polyurethane production[22], as well as for the Baylis-Hilman reaction[23]. It has also featured as a key structure in many studies relating to polycation synthesis, with both mono- and di-substituted structures having been produced for a variety of uses[e.g.24–31], as well as featuring increasingly in ionic liquids[32,33].

In recent years, DABCO has been tested within a H_{cat} pulp bleaching stage, providing highly efficient removal of chromophores in a fast and mild stage at a range of pH values[17–19]. Bleaching results are shown to be improved via the derivatization of DABCO, such as in the use of CM-DABCO, which incorporates a carbomethoxy group (Figure 2)[34].

The aim of the present work is to study the stability and activity of DABCO-based catalysts, during the reaction of HOCl with unsaturated organic substrates. This is with the aim of finding the effect of catalyst structural changes, in order to produce an optimal structure for future testing within bleaching stages, as well as in other potential uses. The impact of the pH and the organic substrate structure are also to be investigated.

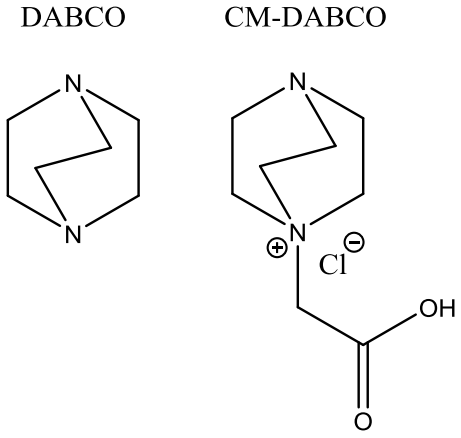


Figure 2: The structures of DABCO and CM-DABCO.

Literature Review

In order to be able to consider the activity and stability of the tertiary amine catalysts in HOCl, it is important first to investigate a number of areas. This includes the basic chemistry of HOCl, as well as the factors affecting its reactions with organic substrates, including the use of catalysts. As well as this, the uses of HOCl need to be investigated, to understand the potential applications of any catalysts developed.

In terms of the tertiary amine catalyst themselves, to select suitable structures for testing, criteria need to be set that define the structures that are of interest in this study. As such, previously synthesized DABCO-derivatives are to be investigated, and from them selected the catalysts to be tested in kinetic studies. This literature review will thus consider these areas.

1 Basics of Hypochlorous Acid and Tertiary Amine Catalysis

Before any considerations of factors affecting HOCl reactions, or potential uses of HOCl and tertiary amine catalysts, it is important to have a full understanding of the chemistry involved. This will now be discussed.

1.1 Hypochlorous Acid

Hypochlorous acid (HOCl) is a strong oxidizing and chlorinating agent. It exists in an equilibrium with hypochlorite ions ($^{-}$OCl), with a pKa of 7.58,[1] meaning that it is the dominant species at a pH below that value, whereas hypochlorite ions dominate above it. While HOCl is an electrophilic oxidizing agent, $^{-}$OCl generally behaves instead as a nucleophilic species, and is a weaker oxidizing and chlorinating agent than HOCl.[35]

At pH values lower than around 3, other free chlorine species also become important in the reactions with organic substrates, particularly Cl_2, but also with Cl_2O present in low concentrations.[2] The electrophilicity of these are greater still than HOCl, and the effects of these other free chlorine species will be discussed more in Section 2.2.

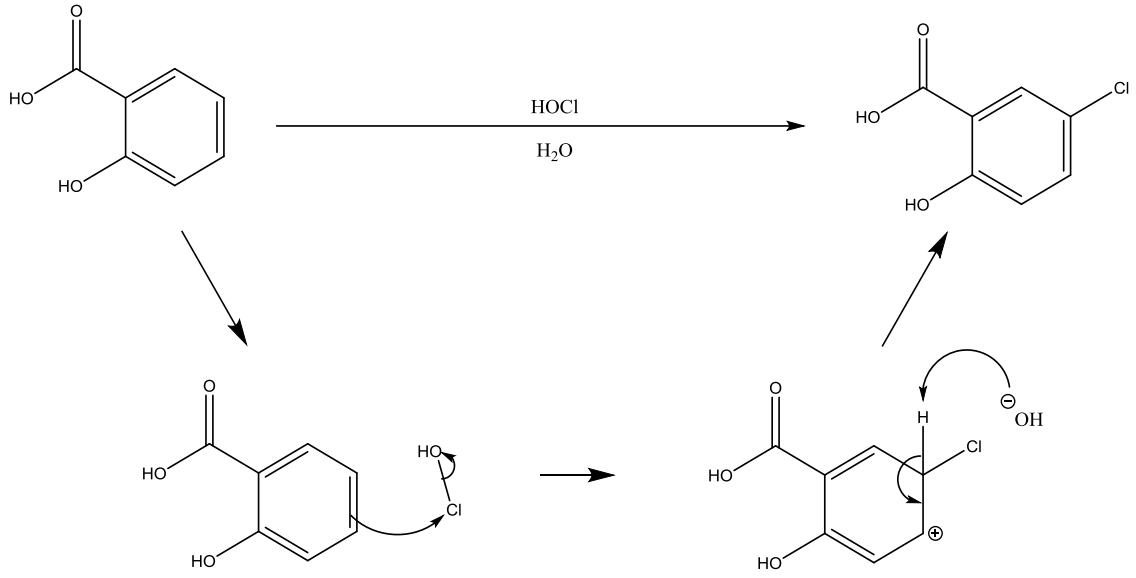


Figure 3: The mechanism of the chlorination of salicylic acid with HOCl.

As an electrophilic reagent, HOCl reacts with electron rich, nucleophilic regions of molecules. It therefore can oxidize alcohols[14], as well as chlorinate amines and sulphur groups[36,37]. Of particular importance in this work is its ability to chlorinate and oxidize alkenes and aromatic compounds[5,6]. An example chlorination reaction mechanism is shown in Figure 3. Here the hydroxyl ion produced acts as a base, deprotonating the cation to reform the aromaticity (substitution reaction), but can also act as a nucleophile (addition reaction), particularly when no aromaticity is involved.

Unlike other oxychlorine molecules, such as ClO_2, HOCl does not react by radical means, except when exposed to superoxide[37], or otherwise in conditions that can cause homolytic O-Cl bond cleavage, such as temperature, UV-light and transition metals[38].

1.2 Tertiary Amine Catalysis

The use of tertiary amines to catalyse the oxidation and chlorination reactions of HOCl is still an emerging area, despite being extensively studied and reported about by Prütz in 1998[16]. The catalysis works due to the rapid formation of a chlorammonium cation, as in Equation 3, which is a stronger electrophile than HOCl itself.

Unsaturated nucleophilic groups hence react more rapidly with it than with HOCl, with $k_4 >> k_5$, resulting in their chlorination and regeneration of the tertiary amine.[16]

$HOCl \leftrightarrow ClO^- + H^+$ (1)	k_1 Hypochlorous acid deprotonation.
$NR_3 + H^+ \leftrightarrow R_3NH^+$ (2)	k_2 Catalyst protonation.
$NR_3 + HOCl \leftrightarrow R_3N^+Cl + HO^-$ (3)	k_3 Chlorammonium cation formation.
$R_3N^+Cl + Org \leftrightarrow Org^+Cl + NR_3$ (4)	k_4 Chlorination by chlorammonium ion.
$HOCl + Org \leftrightarrow Org^+Cl + HO^-$ (5)	k_5 Chlorination by HOCl.

The kinetics of catalysed HOCl reactions can be quite complex. Generally, there are several reactions capable of happening simultaneously, with the balance between them determined by their rates. These reactions include those shown in Equations 1-5, with the catalyst denoted with NR_3. Further reactions of the substrates following chlorination, such as reformation of aromaticity, hydroxyl ion addition or substrate degradation, are not shown, but would also influence the system. There may also be competing areas of reactivity in the organic substrate, such as *ortho* vs *para* chlorination in aromatic compounds like salicylic acid[35].

It can be noted also that HOCl is capable of reacting with not just tertiary amines, but additionally with primary and secondary amines to generate chloramines, of structures NR_2Cl, $NRCl_2$ and NCl_3.[39] For example, when NH_3 and HOCl are together in aqueous solution, such as during water treatmeant, all three of these chloramine structures readily form, as eventually do many non-chlorinated compunds such as N_2 (hence oxidation of NH_3 to N_2 occurs[40].) Chloramines also readily form from amino groups[9].

Research into the mechanisms and kinetics of these reactions has been undergone[41], but whilst these chloramines are capable of further reaction with unsaturated substrates, such as NADH in mammalian cells, they oxidize slower than the HOCl itself, and may not be regenerated[21]. As such, only tertiary amines are of consideration in the current work. The oxidation by primary and secondary chloramines can also be catalysed by tertiary amines however, meaning their existance should be remembered when alongside a tertiary amine presence[21].

2 Factors Affecting HOCl Reactions with Organic Substrates

There are a variety of factors that have an effect on the reactions between HOCl and organic substrates. Whilst the inorganic reactions of HOCl, such as the reaction with chlorite to reform chlorine dioxide, are also well documented, these will not be considered here[42,43]. These factors include the structure of the organic substrate itself, the pH used, the ratio of HOCl to substrate and the use of a catalyst, amongst others. When a tertiary amine catalyst is deployed, the structure of this also affects its activity and stability. The factors affecting the reactions will now be discussed.

2.1 Substrate Structure

Many different substrates have been utilised in the study of the rate of HOCl oxidation and chlorination reactions. Particularly studied are biological substrates, including for example; glutathione and ascorbate[37], amino acids including tyrosine[44], cysteine and methionine[45], flavonoids[46], mononucleotides[16] and lipids[47]. Tests have also been performed on simpler chemical structures, such as polyvinyl alcohol[48], pyruvate[49], salicylic acid[16] and lignin model compounds[50]. Some of these are shown in Figure 4.

A range of rates is obtained depending on the substrate, with factors such as the substrate pKa, steric hindrance around the unsaturation and electronic effects (for example conjugation) affecting not just the rate, but also the product spectrum obtained. Whilst some structures can undergo simple chlorination, such as salicylic acid, others may be oxidized and have a wide-product spectrum, such as with syringol[35,50]. Aromatic and alkene substrates also have major differences in reactivity.

2.2 pH

The effect of the pH on the rate of HOCl reactions is a result of the balance of the two equilibria discussed previously (Section 1.1). At higher pH values, where pH approaches the HOCl pKa of 7.58[1], the equilibrium with hypochlorite (Equation 1) begins to play a role in the reaction, with hypochlorite ions reacting as nucleophiles, and generally as a slower oxidizing agent than hypochlorous acid.

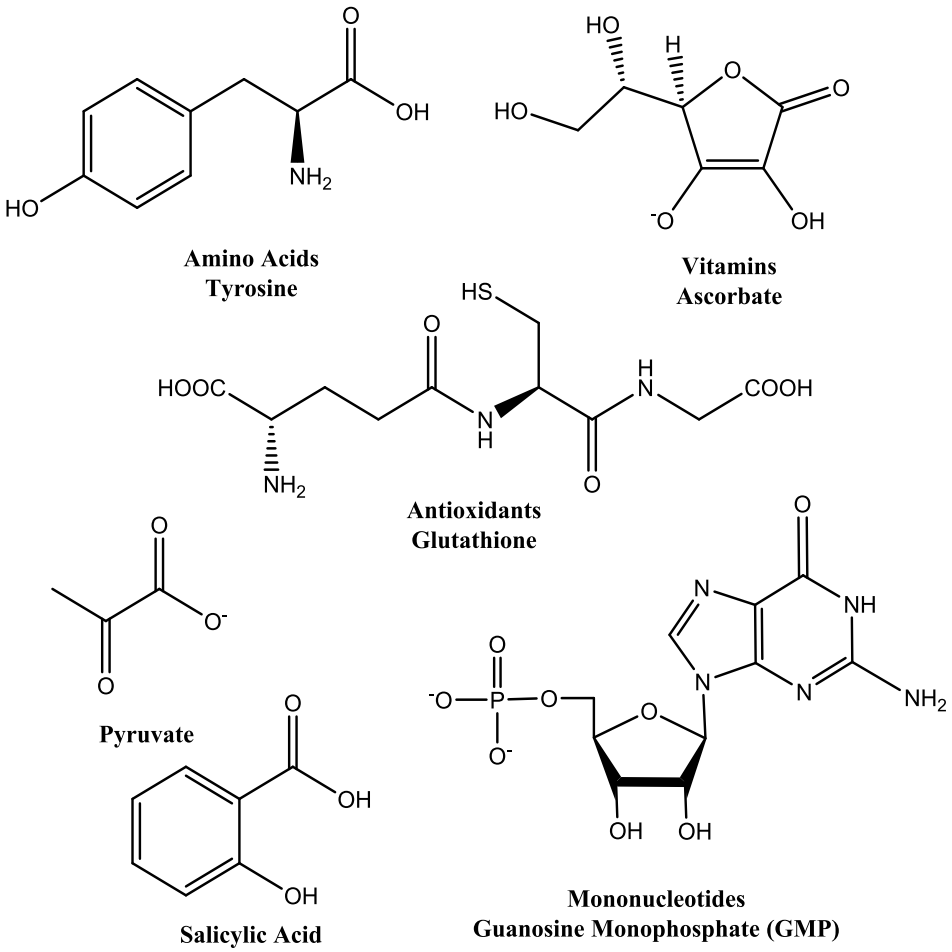


Figure 4: Examples of some of the structures that have been shown to react with HOCl.

Evidence of this can be seen from Broadwater et al., who found that both the rate of salicylate chlorination is decreased by pH changes between 6.2 and 8.6.[35] This relates to a direct increase in the concentration of hypochlorite ions, until they become the dominant species at a pH of 7.58.

However, the substrate and catalyst structures can also affect this, in particular in regards to their pKa values. As investigated by Sivey et al., when the substrate used is phenol, the maximum rate of reaction with free chlorine is instead at pH 8.6, which is approximately the midpoint between the pKa of HOCl (7.58) and phenol (9.95).[2] This therefore is where there is the combined maximum concentrations of HOCl, which is more electrophilic than $^{-}$OCl, and of the phenolate ion, which is more nucleophilic than phenol. Salicylic acid, with a phenol pKa of 13.4, also increases at pH above 8.6 for this reason, as the concentration of phenolate equivalent increases[51].

Abia et al. also displayed that when the reaction being considered is instead the chlorination of amines, rather than unsaturated groups, the structure of the amine changes the magnitude of the effect of pH changes.[39] In all cases the maximum rate is found at around pH 9, but the difference between pH 6 and 9 is around tenfold higher for Me_2NH than it is for $(i\text{-}Pr)_2NH$.

The second equilibrium of importance is at low pH, with Cl_2 and Cl_2O concentrations becoming significant at pH values below 3. The equilibrium reactions between these free chlorine species and HOCl are shown in Equations 6 and 7.

$$HOCl + Cl^- + H^+ \leftrightarrow Cl_2 + H_2O \quad (6) \qquad k_6 \text{ Formation of } Cl_2 \text{ from HOCl at low pH.}$$

$$2HOCl \leftrightarrow Cl_2O + H_2O \quad (7) \qquad k_7 \text{ Formation of } Cl_2O \text{ from HOCl.}$$

The relative rate between these and HOCl is substrate and reaction dependent, but Cl_2 reacts generally at a far higher rate than HOCl due to its higher electrophilicity, with Cl_2O in between in reactivity terms, due to its improved leaving group ability compared to HOCl[2]. In the chlorination of Me_2NH for example, the reaction rate is close to thirtyfold higher for Cl_2 than for HOCl[39].

The ratio between the significance of the free chlorine species is also dependent on the organic substrate structure. When considering methoxybenzene structures, the relative importance of Cl_2O and Cl_2 increases with a decreasing reactivity (nucleophilicity) of the methoxybenzene.[2] This is a result of a higher electrophilicity becoming increasingly important when reacting with a nucleophile of lowered nucleophilicity.

When a tertiary amine catalyst is utilised, the reactions of Cl_2 and Cl_2O may not proceed via the chlorammonium cation structure, lowering the catalytic effect. As mentioned however, this will depend on the substrate nucleophilicity, with a more reactive substrate reacting in larger amounts with HOCl.

2.3 Component Ratios

The relative concentrations of the components of the reaction, meaning HOCl, organic substrate and tertiary amine catalyst, also have an impact on the reaction rates, as well as in some cases on the selectivity between possible reactions.

Although HOCl is the oxidizing agent in use within this work, other oxidizing agents that perform in a similar manner can also be considered in observing how HOCl reactions behave. Ozone, like HOCl, is an electrophilic oxidizing agent and so can provide a good analogy. Pipon et al. found that the ratio of oxidant:substrate has a direct impact on the maximum absorbance (hence highest rate of formation) of a range of phenolic compounds such as vanillin and syringol.[52] The maximum absorbance was found to increase steadily up to a ratio of 1.5 ozone:substrate, before decreasing first slowly up to a ratio of 3.5, and then more sharply at higher ratios.

The ratio of the substrate and HOCl can also have an effect beyond simply the rate of reaction. Krych-Madej et al. tested the mechanisms of the reaction of HOCl with plant flavonoids (polyphenolic compounds), and determined that the molar equivalence of HOCl is a key factor in the kinetics and mechanisms of the reactions.[46] They concluded that oxidation is performed on the flavonoid compounds only when a molar excess (>10) of HOCl is used, and below this chlorination is the favoured pathway.

In terms of the catalyst concentration, Prütz et al. found that an increase of the catalyst (trimethylamine) concentration produces a linear increase in the rate of reaction of the chlorination of salicylic acid[16]. This was tested up to a substrate:HOCl:catalyst ratio of 200:20:1.

2.4 Buffer Type

In kinetic studies of HOCl, buffer solutions are required to avoid pH changes that come about from the generation of ^{-}OH during chlorination. It has been shown that the use of a phosphate buffer, which is generally used to buffer at pH 7, increases the rate of chlorination of salicylic acid, showing it in some way participates in the chlorination reaction.[35] Hence, increasing the concentration of the phosphate buffer also increases the reaction rate.

Buffers such as citrate, borate and carbonate do not affect the reaction rate, and hence a mix of them can be preferable to a phosphate buffer in the case of wanting direct comparison of rates between different pH values[35].

2.5 Catalyst Use and Structure

There are two factors that are affected by the structure of the tertiary amine catalyst. The first of these is the activity of the catalyst, and hence the rate of the reaction produced from their use. The second is the catalyst stability within the HOCl reaction medium. The studies and conclusions of both of these factors will now be presented. All catalyst structures discussed within this section can be seen within Figures 4 and 5. Those shown to be capable of catalytic activity are shown in Figure 4, whilst those that are not capable are in Figure 5.

2.5.1 Effect on Activity

In one of the first works investigating the catalytic effect of tertiary amines, Prütz at al. studied the effect of changing the structure of the tertiary amine on the rate of reaction with salicylic acid, sorbate and mononucleotides.[16] The tested tertiary amines included trimethylamine (TMA), quinine, quinuclidine and 2-[N-morpholino] ethanesulfonic acid (MES). They concluded that quinine has the highest activity of these catalysts, due to the quinuclidine substituent and it's highly available amine group. Quinine catalyses more effectively than quinuclidine itself, with TMA and MES between the two. Other quinuclidine derivatives have also displayed catalytic

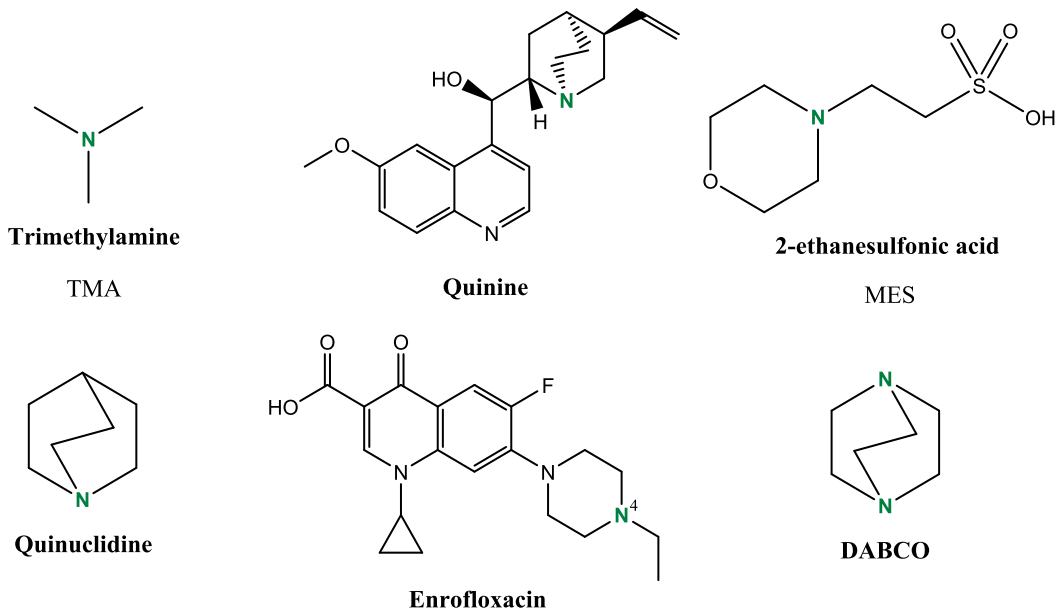


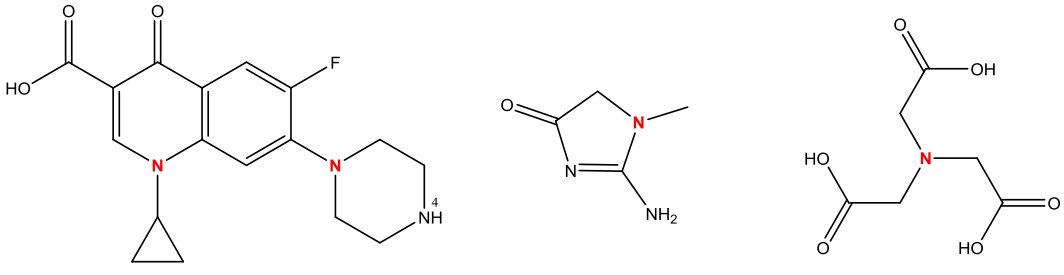
Figure 4: Tertiary amine structures shown to be capable of catalyzing HOCl reactions.

ability in NADH oxidation[21]. Primary, secondary and quaternary amines displayed no catalytic properties.

The effect of changing the tertiary amine structure was investigated also by Shah et al.[20] This was in terms of the removal of organic matter (and increased by-product formation) when tertiary amines are included in water treatment. They found that whilst TMA and MES enhance the removal of organic contaminants, creatinine and nitrilotriacetic acid were ineffective, again displaying that the nature of the tertiary amine does majorly impact its ability as a catalyst.

To achieve catalytic ability, it is likely important that the tertiary amine is not a part of a conjugated system. Dodd et al. found that whilst enrofloxacin (Figure 4) had catalytic ability, ciprofloxacin (Figure 5), which differs only by having one less substituent on the N(4) amine, does not[53]. This hence shows the other tertiary amines, both of which are adjacent to unsaturated bonds, are not capable of performing as catalysts, or at least perform ineffectively. This is also the case in creatinine, tested by Shah et al.[20]

As can be seen in Figure 4, the tertiary amines that have shown activity as catalysts all feature a cyclic tertiary amine, with TMA the only exception. The lone pair of the amines in these cyclic groups suffer less steric hindrance from neighbouring groups than free tertiary amines, and hence are more nucleophilic. TMA, whilst not cyclic, also only has small methyl groups bound, which only slightly sterically hinder the amine lone pair, compared to for example in nitrilotriacetic acid, which shows no catalytic ability partially due to steric shielding[20]. Nitrilotriacetic acid also has three acetyl groups withdrawing electron density from the amine, so has both a sterically



Ciprofloxacin Creatinine Nitrilotriacetic acid

Figure 5: Tertiary amine structures shown to be incapable of catalyzing HOCl reactions.

and electronically unavailable lone pair. Overall, an available lone pair results in faster chlorammonium cation formation and hence a better catalytic potential.

The basicity of the catalyst also has an effect on the pH dependence of the reaction.[16] When using a lower basicity catalyst, such as MES with a pKa of 6.15, and increasing the pH even from 7.2 to 8.1, the rate of chlorination markedly drops by over twentyfold. This is in contrast to a catalyst with higher basicity, such as quinuclidine with a pKa of 11, with which the rate doubles from the same pH change. Hence, moving closer to the catalyst pKa has a positive effect on reaction rate.

2.5.2 Effect on Stability

Considering the catalyst stabilities, as discussed by Prütz et al., when tertiary amines (TMA in this case) are pre-incubated for several minutes with HOCl prior to mixing with the salicylate substrate, no reaction can be observed.[16] A large catalyst excess also has similar effects. Prütz attributes this to autocatalytic reactions of the chlorammonium species with the tertiary amine (TMA^+Cl and TMA), which is increased either by retention time or by free catalyst amount available to initiate decomposition of the chlorammonium species. Quinine does not appear to undergo these reactions.

Another display of the effect of the catalyst structure on stability was in the bleaching of pulp in a H_{cat} stage (Section 3.1). Here, the change from a DABCO catalyst to a DABCO derivative, CM-DABCO, provided increased bleaching outcomes and allowed for lower concentrations of active catalyst being required[18,19,34]. The reasoning for this was concluded to be DABCO undergoing rapid decomposition in the bleaching process, in the same way as TMA. Rosenblatt et al. have previously investigated the kinetics of DABCO degradation in HOCl also[54].

Overall it is important that the catalyst used does not undergo decomposition within the reaction medium, as well as having an available tertiary amine lone pair, that is not involved in a conjugated system or sterically shielded. It also is likely a pKa near the pH of the reaction is desirable.

3 Uses of Hypochlorous Acid

As discussed, hypochlorous acid and hypochlorite ions are widely used oxidizing agents, for purposes that include disinfection, within chemical synthesis to oxidize alcohols and alkenes and as a traditional wood pulp bleaching stage. These uses will now be discussed, with a focus on those relevent and promising in regards to their use in conjunction with tertiary amine catalysts.

3.1 Wood Pulp Bleaching

Chemical bleaching forms the most expensive area, both economically and environmentally, of the production of bleached chemical pulp. Generally, 3-5 stages are involved, together forming the bleaching sequence.[55] Stages commonly used include oxygen (O), acid hydrolysis (A), ozone (Z), chlorine dioxide (D) and hydrogen peroxide (P).

The aim of bleaching is to remove the coloured structures present within pulp. Lignin is the primary one of these, being the second largest component of wood overall, following only after cellulose.[56] The structure of lignin is macromolecular, formed from the three alcohols shown in Figure 6, joined by a variety of bonds.

Hexenuronic acid is formed from the elimination of methanol from 4-O-methylglucuronic acids during the kraft cooking process, and is the other compound aiming to be removed[57]. Despite not itself being a chromophore, results have shown

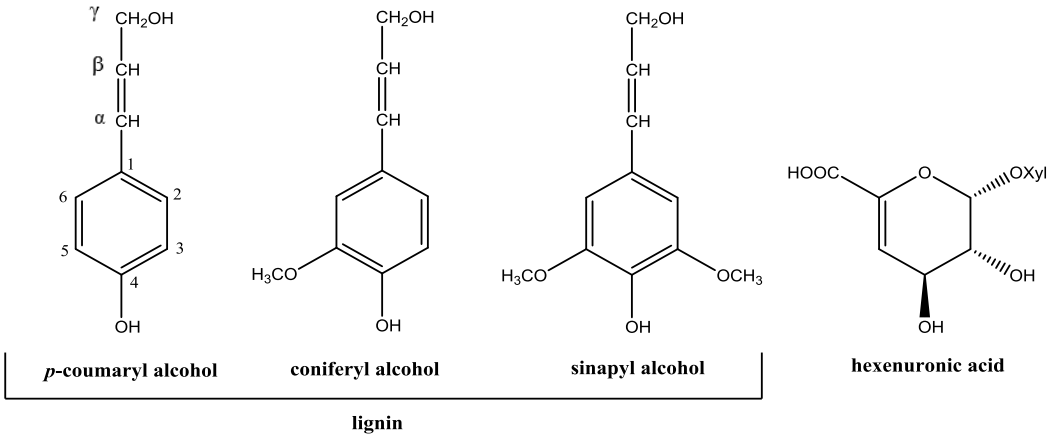


Figure 6: The structures of the compounds aiming to be removed in the bleaching process.

previously that it has chromophoric degradation products, as well as contributing to kappa number (κ) calculations, hence meaning it too is important to remove[58].

3.1.1 H and H_{cat} Stages

Hypochlorite bleaching (H-stage) is one of the oldest treatments in the bleaching of pulp.[7] This traditionally was used as a final bleaching stage, at alkaline pH, meaning it utilised nucleophilic hypochlorite ions in order to oxidize the highly electrophilic coloured quinonic groups. This stage has now been replaced by the use of a hydrogen peroxide stage, which results in far lower amounts of chloroform and AOX formation[55].

As HOCl is an electrophilic agent, it reacts rapidly with the electron rich elements of lignin and HexA. Phenols, as found within lignin, are highly electron rich due to the electron donating effect of hydroxyl and ether groups, as is the carbon-carbon double bond of HexA. These are then prone to reaction.

In recent years, tertiary amine catalysis has been tested in the bleaching of wood pulp, within a H_{cat} bleaching stage[17–19,34]. High levels of lignin and hexenuronic acid (HexA) removal can be achieved from eucalyptus pulp, using the tertiary amine (DABCO) combined with hypochlorous acid (H_{cat} stage)[18]. Additionally, when a pH below 6 is used, only low amounts of chloroform, AOX and OX are formed in comparison to the generally used chlorine dioxide bleaching[17]. Studies using UV-Raman spectroscopy have shown the H_{cat} stage removes greater relative amounts of HexA than lignin, showing this is the primary positive effect of the stage[19,34].

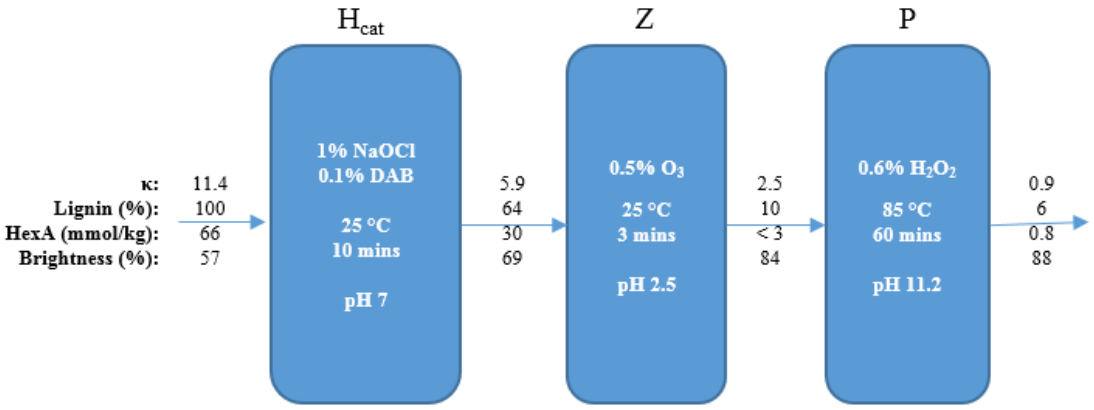


Figure 7: The optimal tested conditions and results of the H_{cat}ZP bleaching sequence.

This stage also involves fast reactions, allowing for low retention times in the bleaching process, especially when combined with other short bleaching stages such as ozone (Z) and hydrogen peroxide (P)[19]. Fully bleached pulp has been shown to be achieved from a H_{cat}-Z-P sequence, as in Figure 7[19].

Similarly to this H_{cat} stage used, DABCO has also been utilised together with enzymes in an alternative pulp bleaching sequence.[59] In this, DABCO acts as a co-catalyst with the vanadium haloperoxidase enzyme (Hap), with HOCl still acting as the oxidation agent. HOCl in this case however is formed *in situ*, via the addition of H_2O_2 and NaCl, a reaction that is catalysed by Hap. The stage takes place in a buffered pH 4.5 solution. This has also resulted in an efficient stage, producing high rates of lignin and HexA removal without significant cellulose degradation.

3.1.2 D and D_{cat} Stages

One of the most common pulp bleaching stages used in modern day pulp mills is the chlorine dioxide (D) stage.[55] This has largely replaced Cl_2 as a bleaching agent, resulting in elemental chlorine-free (ECF) bleaching, which has had a positive effect on the environmental sustainability of pulp mills, with a far lower level of environmentally damaging chlorinated products being released. It has also lowered costs and increased the quality of product. It does however require the usage of large bleaching towers and long retention times, as well as being inefficient in regards to active chlorine charge. Hence, there is the potential for it to be improved further.

Unlike the electrophilic hypochlorous acid, chlorine dioxide (ClO_2) reacts through radical reactions.[42,55] This results in it being extremely efficient in the oxidation of lignin, rapidly degrading it into a range of water soluble products such as acetic and muconic acid[50]. It is performed in acidic pH, generally between pH values of 3 and 5.

The D-stage is relevant here, due to HOCl being a secondary reaction product produced during the ClO_2 bleaching treatment.[42] In Figure 8 is shown the oxychlorine reaction scheme operating during D-stage pulp bleaching.[43] As can be seen, HOCl plays a key role, contributing to the oxidation and chlorination, and hence depolymerisation, of lignin, as well as the degradation of HexA. It also reacts with chlorate to reform the chlorine dioxide, allowing for a lower needed ClO_2 charge.

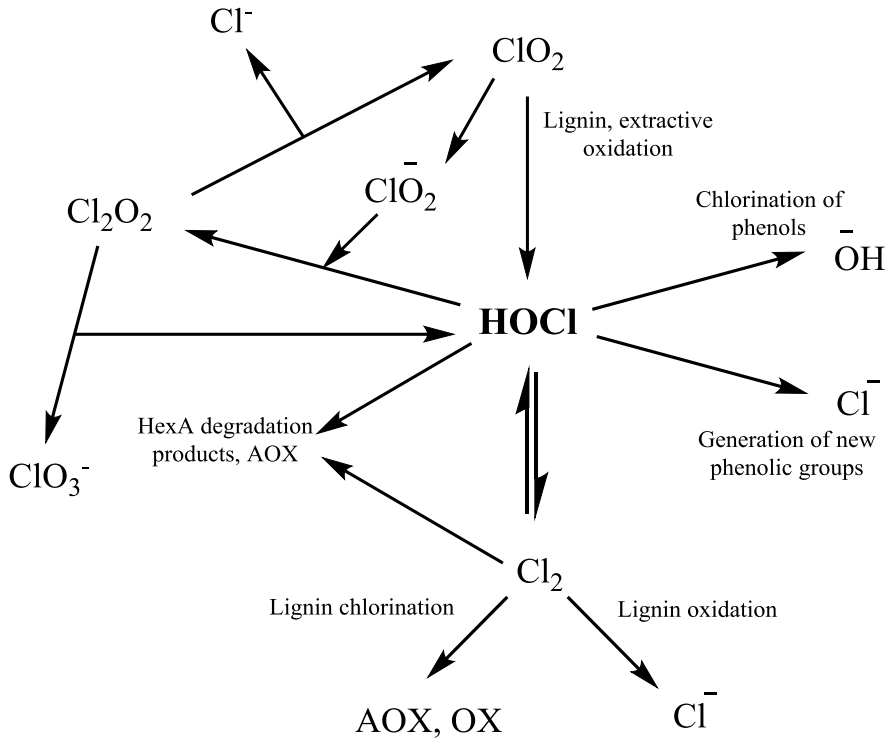


Figure 8: The oxychlorine bleaching reaction scheme.

It is therefore hoped that the D_{cat} stage can also be significantly improved by the use of tertiary amine catalysts, by catalysing both the organic reactions between HOCl, HexA and lignin, as well as the inorganic ones that reform chlorine dioxide. This would help to overcome the long retention times required for D-stage bleaching, as well as decreasing the effective chlorine charge needed. Work published previously has displayed that DABCO is unsuitable for these uses, undergoing degradation in the presence of ClO_2, but otherwise there is currently no published literature of the use of a D_{cat} stage[60]. Ultimately however, the tertiary amine catalysis of HOCl has a good potential to reduce both the environmental and economic costs of pulp bleaching.

3.2 Biocides and Water Disinfection

3.2.1 Reactions with Biological Substrates

The reactions between HOCl and a variety of biological substrates have extensively been studied. Within mammalian cells, myeloperoxidase enzymes react Cl_2 and H_2O_2, to generate HOCl, as a means of killing harmful pathogens, as shown in Equation

7.[61,62] This HOCl formation is vital for health, but errors in expression, or other reasons for overly large amounts of HOCl, has been shown to contribute to tissue injury[63].

$$H_2O_2 + Cl^- \leftrightarrow HO^- + HOCl \quad (7) \qquad k_7$$ Myeloperoxidase catalyzed HOCl formation.

The reaction of HOCl with a variety of biological substrates has hence been studied, including with DNA[64], mononucleotides[9], amino acids and proteins[65], unsaturated fatty acids[47], haemoglobin[66] and thiols[9,61]. Results have shown that sulphur containing compounds are particularly vulnerable to reaction with HOCl. Unlike just the unsaturated group oxidation that is of interest in this work, there are many different possible types of reaction that are possible, including chloramine formation from reactions with amino groups.[9] These chloramines are long-lived and capable also of microbicidal activity, extending the bioactivity of HOCl.

The effect of tertiary amines on these reactions has also been tested, including in the initial work discussing the phenomena, where reaction with sorbate and nucleotides were tested[16]. Although the reactions with biological substrates currently provide no uses for tertiary amines, it is this high HOCl reactivity that also leads well to the antibacterial properties of NaOCl[61]. Biological substrates are also common precursors to a wide range of products, including pharmaceuticals and cosmetics, so the creation of more catalysed reactions to change the structure of these could be a huge future benefit.

3.2.2 Use as a Biocide

NaOCl is a utilised biocide for various purposes, most notably as a household disinfectant. Within chlorination water disinfection, HOCl is a key species, and is present in a concentration several orders of magnitude higher than Cl_2.[35] During water disinfection, some organic contaminants are chlorinated, for which HOCl is considered to be the principle source, with contribution from both Cl_2 and Cl_2O also[67].

Tertiary amines are a common product to enter the water system from various industrial applications, and hence the effect of them on the water disinfection has been tested. It was found that when present, they can improve the rate of organic contaminant loss and disinfection by-product formation[20].

Chloramination steps are also regularly utilised in modern wastewater plants, which feature the introduction of ammonia and subsequent formation of chloramines during water treatment.[40,68] This produces fewer toxic side products during the disinfection than within chlorination steps.

Polycationic structures based off DABCO, as well as other tertiary amines, have been tested previously for their antibacterial and antifungal uses[24–27]. Currently however, tertiary amines used in combination with HOCl have not been tested in a similar way as the chloramination step, with a major challenge coming from their use being their high water toxicity, meaning they themselves have to be removed completely. Thus a method such as the grafting of tertiary amines onto a stationary surface is one possibility, although some leaching would still occur. Alternatively a structure that is capable of degrading into non-toxic products would be an option.

3.3 TEMPO Oxidation of Alcohols

2,2,6,6-Tetramethylpiperidinyloxy (TEMPO) is a commonly used tertiary amine reagent for the oxidation of primary and secondary alcohols to aldehydes and ketones respectively[13,14,69]. It has also been utilised within the oxidation of cellulose and hence production of nanocellulose[70]. The general scheme for TEMPO oxidation is displayed in Figure 9.

As can be seen, HOCl plays a very different role within this system compared to other tertiary amine-HOCl systems discussed, not least because of the high pH used meaning $^{-}$OCl is the dominant species[69]. Here, a chlorammonium species is not formed, but rather $^{-}$OCl acts as a secondary oxidant, converting Br^{-} to $^{-}$OBr, which in turn regenerates by oxidation of the active TEMPO species[13]. The oxidation of Br^{-} with hypochlorite has been studied previously[71]. The removal of NaBr, meaning hypochlorite ions would oxidizing the TEMPO directly, would be an improvement to the environmental aspect of the process, but also greatly lowers oxidation rate, unless elevated temperatures are used[72].

Work has been performed previously however on the replacement of NaBr in the TEMPO system, specifically when oxidizing cellulose to produce nanocellulose; with

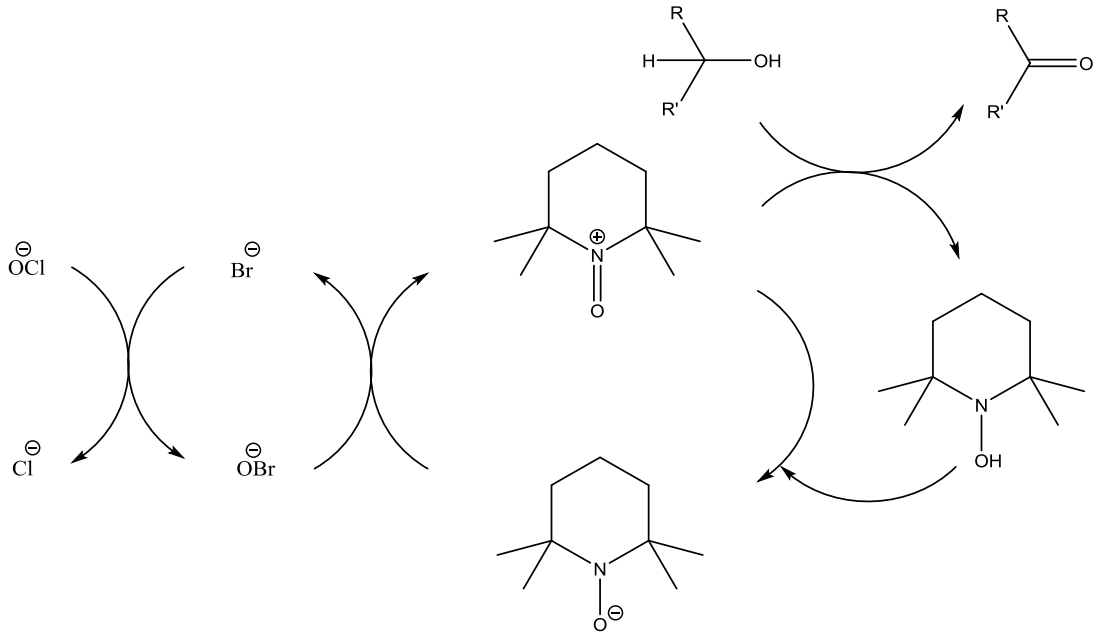


Figure 9: The catalytic cycle for TEMPO oxidation of primary and secondary alcohols.

pretreatment by HOCl, ClO_2 and alkali all being tested and proved effective[73–75]. The use of a tertiary amine is also a currently untested option.

The reasoning behind the use of NaBr is that the $^{-}$OBr generated by the reaction between NaBr and $^{-}$OCl is a more reactive than $^{-}$OCl, and hence more rapidly regenerates the TEMPO active species[35]. As discussed, the chlorammonium species formed is also significantly more reactive than HOCl/$^{-}$OCl, and as such could potentially act as a replacement to the $^{-}$OBr formation[16]. This therefore is an area where development of a more stable and active tertiary amine catalyst could have benefits, for both the general oxidation of alcohols, and in the production of nanocellulose. The high pH would mean a very different catalyst structure would be needed than for lower pH uses however, and chlorammonium formation is also expected to be slower with hypochlorite ions than with hypochlorous acid.

An alternative method of involving the tertiary amine-HOCl system in TEMPO usage is via the use of a H_{cat} bleaching stage (Section 3.1.1) prior to the TEMPO step, in the production of nanofibrillated cellulose (NCF)[76]. This mild H_{cat} bleaching, with DABCO as a catalyst, followed by an alkaline pretreatment, is able to remove much of the xylan that is found distributed unevenly on the cellulose surface. This overall results in a NCF aerogel with improved properties, as xylan is strongly water binding, thus increasing swelling and weakening the overall structure of the aerogel. A

modified catalyst then could possibly more efficiently remove the xylan, resulting in a further improved aerogel, or one that can be produced in milder conditions.

3.4 Oxidation of Alkenes

Tertiary amines were not the first catalysts used for reactions of NaOCl with unsaturated molecules. NaOCl has also found widespread use as an oxidizing agent for the epoxidation of alkenes, particularly asymmetric epoxidation - epoxidation with a high enantioselectivity, with the use of Mn-salen based catalysts[77]. In the early 1990's, Zhang et al. developed this method, utilising NaOCl and an Mn-salen catalyst to produce epoxides with a high selectivity[6]. The enantioselectivity of these catalysts relies on restricting the route taken by the substrate to the active catalyst, the Mn(V) species with bound oxygen, via the use of bulky side groups[12]. This causes one route to be heavily favoured, resulting in reaction from one face of the alkene only.

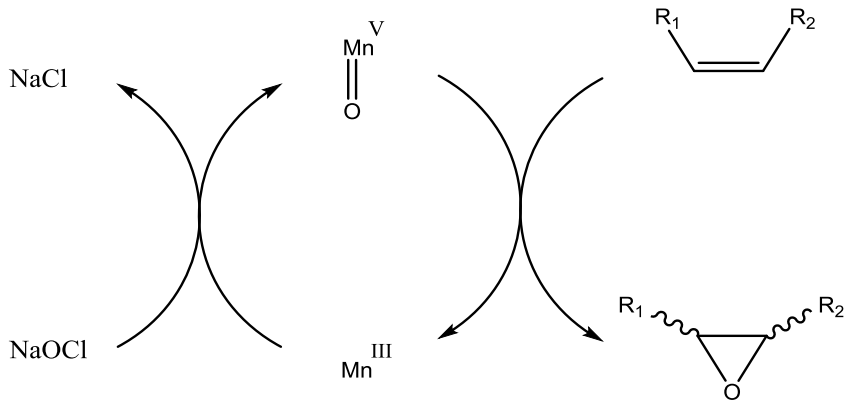


Figure 10: The catalytic cycle of Mn-salen catalysts with NaOCl in alkene epoxidation.

One interesting property of these catalysts is that by varying their side groups, different enantiomers of the final epoxide can be favoured by directing the substrate along different routes. Although NaOCl is used here however, the method of action is considerably different than that with tertiary amine catalysis, meaning direct comparisons are difficult. It is however interesting to note that NaOCl can be a selective enough oxidation agent to be capable of enantioselective oxidation, when combined with the right catalyst, and this could potentially include a tertiary amine. Enantioselective synthetic routes using tertiary amines are then a future possibility.

4 Catalyst Structure Considerations

DABCO is a commonly used industrial catalyst for the synthesis of polyurethanes, as well as in the Baylis-Hilman reaction[22,23]. A reason for the success of DABCO in tertiary amine uses is due to its high nucleophilicity (with a relatively low basicity at pKa_1 of 8.82.)[78] This is due to its rigid structure; the nitrogen lone pairs project out into empty space, with no groups available to block access to them, and hence are highly nucleophilic, as shown in Figure 11. Additionally, as a diamine, the reaction is statistically favoured compared to monoamine structures such as quinuclidine[78].

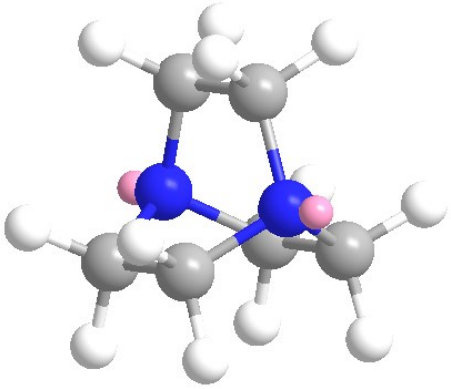


Figure 11: The 3D structure of DABCO, with the nitrogen lone pairs being shown in pink.

This high nucleophilicity, as well as it having been shown previously in bleaching studies to exhibit efficient lignin and HexA removal (Section 3.1), means that it can be considered as an ideal starting point for the development of tertiary amine catalysts.[18] As such, here the only tertiary amine base structure that will be considered is DABCO.

Another advantage of the DABCO structure is the proximity of the nitrogen atoms allowing for the addition of a derivative to one significantly affecting the reactivity of the other.[29] This allows for modifications to one nitrogen of the structure to be made, whilst still leaving an amine group free. When the nitrogen atoms are further separated, it is far harder to selectivity modify one of them only, as the nature of one doesn't have such a direct effect on the other[79].

Within this section, the reasoning for the derivatization of DABCO will be discussed, followed by setting criteria of the structures that are of interest in this work, in order

to narrow down the large amount of structures previously synthesised. Finally, the catalysts fitting this criteria will be found and discussed.

4.1 Reasoning for DABCO Derivatization

Compared to the base DABCO structure, previous work has displayed that the pulp bleaching efficiency within the H_{cat} stage is improved greatly by the derivatization of one amine group, producing a tertiary ammonium chloride salt, and leaving one free amine to partake in the catalytic cycle.[34]

The main reasoning for this has been established to be due to the degradation of DABCO within HOCl solutions, as discussed in Section 2.5.2. Within HOCl bleaching conditions, DABCO degrades rapidly, reducing active catalyst concentration and decreasing overall catalytic ability (hence worsening the bleaching outcome)[18,54]. It is believed that by forming an N-derivative of DABCO, these autocatalytic reactions can be lessened, increasing catalyst stability and hence bleaching results.

It should also be noted that whilst stability is improved, this is likely not reflected in the initial rate, as the rate of the catalytic reaction is higher than degradation reactions. The diamine nature of DABCO likely results in a higher initial rate in fact[78], but also a shorter catalytic lifetime and hence overall worse performance.

4.2 Criteria of Catalyst Structure Interest

The synthesis of DABCO was first reported in 1942[80], with the first reported derivatives in 1959, where both mono- and di-substituted derivatives were produced[81]. Since then a huge number of derivatives have been synthesised. As such, when considering these structures, some criteria need to be established of those considered of interest and relevance.

The first criteria of structures to consider relates to the DABCO amine groups themselves. In the present work, only derivatives those that are mono-N-substituted will be considered, as only these have the possibility of participating in the HOCl catalytic cycle. Mono-substitution can be achieved by the correct selection of reaction solvent. Within solvents such as ethyl acetate and methylene chloride, the mono-

alkylated salt is no longer soluble, resulting in precipitation upon formation and preventing further reaction[29].

The negative counter ion of the DABCO derivative can also be vastly different, including for example halides, ClO_4^-, PF_6-, CH_3COO^- and TfO^-[e.g.29,33,82]. Catalysts with chloride as the counter ion are of particular interest here, due to the presence already of chlorine atoms in the HOCl-catalyst system, although bromide catalysts will also be mentioned in particular cases when chloride compounds are not available.

One further definition of the derivatives of interest here is based on derivative size. The catalyst previously tested successfully within wood pulp bleaching is CM-DABCO, which features a carboxymethyl group. As such, derivatives particularly of interest are those also of this size, with DABCO in the β- position to the derivative functional group, although larger groups are also considered more briefly.

In summary, DABCO derivatives of interest in this work are those with:

- A substituent present on one nitrogen group only.
- A counter ion to the quaternary amine cation being chloride or bromide only.
- DABCO in the β- position to the functional group, as with CM-DABCO.

4.3 Non-Polar Groups Derivatives

Shown in Figure 12 are previously synthesized non-polar groups that follow the criteria discussed in Section 4.2. As shown, DABCO structures featuring a straight ethyl chain[83], an allyl group[29] and a benzyl group[84] have all been produced.

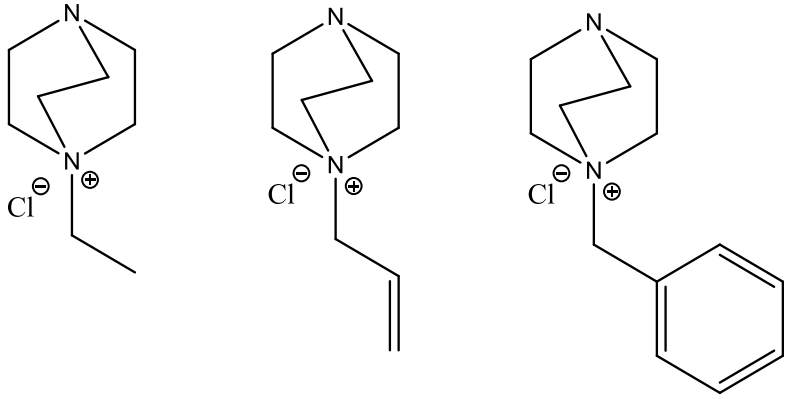


Figure 12: Previously synthesized DABCO derivatives featuring non-polar groups.

An ethyl group has generally not been the favoured carbon chain length introduced, due to larger chains resulting in a charged molecule with a large aliphatic region, as is desired in ionic liquid and lipid uses, meaning that longer chains are more common[29,25,85]. It has however been produced in studies also involving those with longer chain derivatives with both chloride and bromide counter ions[83,86].

Both allyl bromide and allyl chloride have successfully attached an allyl group to a single nitrogen group[29,87], but there have been no cases where propynyl chloride or similar has attached a carbon-carbon triple bond.

Derivatives involving arene groups have been extensively synthesized, particularly benzyl-DABCO, via reactions with benzyl chloride and benzyl bromide.[84,88] Some larger aromatic structures have been also[89].

4.4 Polar Derivatives

Within this work, polar functional groups are separated into those capable and incapable of hydrogen bond donating, for reasons relating to catalyst pKa as explained in Section 6.1.

Of the groups capable of performing as hydrogen bond donors, carboxylic acids[90], amides[82], alcohols[26] and amines[91] have all been successfully attached to the DABCO structure. There have however been no cases of the chloride version of the amine being used, with only the bromide being featured, at a very low yield. Figure 13 displays these structures.

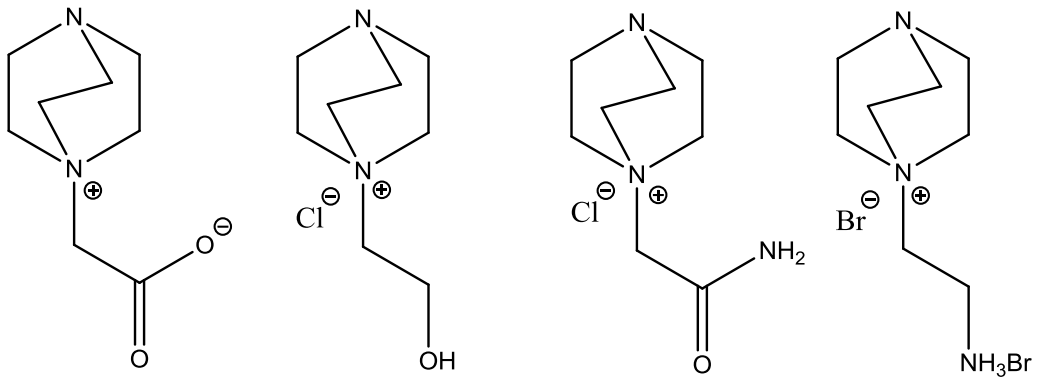


Figure 13: Previously synthesized DABCO derivatives featuring hydrogen-bond donating groups.

Although the carboxylic acid structure, CM-DABCO, is shown as an internal salt, it can also be considered to have a chloride counter ion, due to being formed from the cleavage of a chloride counter ion bound ester group[90]. The amide structure was produced in good yield with chloride counter ion[82], as was the alcohol[26].

Considering then those polar groups not capable of hydrogen bond donating; ketones[92], esters[29] and nitrile[93] groups fitting the criteria have also all been synthesized onto the DABCO core, as in Figure 14.

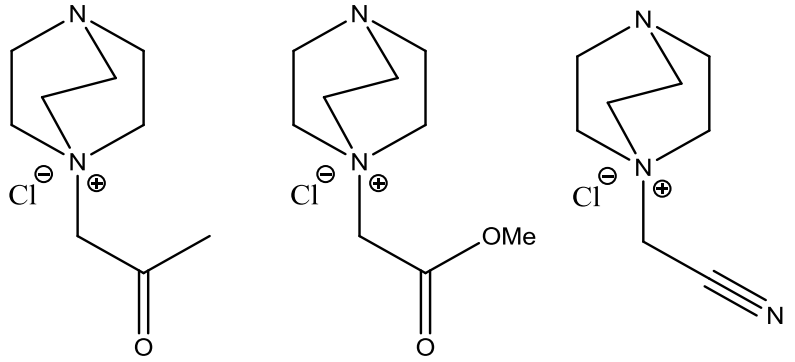


Figure 14: Previously synthesized DABCO derivatives featuring polar groups not capable of hydrogen-bond donating.

The notable polar group not synthesised onto DABCO previously are aldehydes, likely due to chloroacetaldehyde generally existing as an acetal in aqueous conditions, as with many aldehydes. An ester featuring instead a carboethoxymethyl group has also been synthesised, but is not shown[90]. Phenyl ketones have also been produced, but only as an intermediate[94], as have those with the ketone further away from the DABCO molecule[29].

4.5 DABCO Linkages

Work has also taken place investigating the linking together of two DABCO molecules with a range of linkages.[29,31,95–97] This produces an overall 2^+ ion, which therefore may behave differently and have altered properties to those structures discussed previously.

The main form of linkage used to join two DABCO molecules has been pure carbon chains. These range in size from just two carbons, utilising reagents such as 1,2-dibromoethane[97] and 1,2-dichloroethane[31], as is of interest here, to as high as 10 carbon

chains[29,95,96]. These structures generally are synthesized via slow addition of the dihalogenated reagent to DABCO in a solution of a solvent such as acetonitrile. Traditionally, slow addition and low molar equivalences have been used to guarantee correct product formation, however more recently higher equivalences, including 1:2 (dihalide:DABCO), have also been used to good effect[95–97]. High yields have been obtained for all the synthesized lengths of pure carbon chain. Chains with heteroatoms have also been synthesized[29].

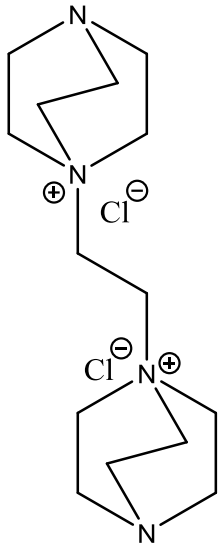


Figure 16: The structure of two DABCO molecules linked by an ethyl group linkage.

5 Conclusions of Literature Review

Hypochlorous acid is an electrophilic compound, capable of reacting with electron-rich areas of molecules. Tertiary amines, such as the diamine DABCO, are capable of catalysing these reactions via the formation of a highly electrophilic chlorammonium cation[16]. The effect of tertiary amine catalysts has been studied in three different areas; in H_{cat} stages in wood pulp bleaching[17–19,34,59], in reactions with biological substrates[16] and in water disinfection[20]. Currently H_{cat} bleaching is the area with ongoing research into the development and use of tertiary amine catalysts, with other uses only currently possibilities. These include their usage in conjunction with TEMPO in the production of nanocellulose, as well as within other organic synthesis uses.

A variety of factors affect the rate of HOCl oxidation and chlorination reactions of organic substrates. This includes the structures of the substrate and catalyst, the pH, the component ratios and the buffer type used. In terms of the catalyst structure, it is important that the tertiary amine is not sterically shielded, not forming part of a conjugated system, and it stable within the HOCl reaction medium. Quinine has thus shown itself to be an efficient catalyst[16]. The amount of work relating catalyst structure and activity remains low however, particularly of the study of the effect of small changes to the overall structure only, as is aimed to be done within this work.

DABCO has been used within H_{cat} bleaching stages, and has been shown to have low stability, a problem which is largely solved by the synthesis of a substituent onto one of the tertiary amines, such as in CM-DABCO[17–19,34]. A H_{cat} stage featuring CM-DABCO has been shown to provide efficient pulp bleaching with only a 0.01% catalyst dose[34].

The catalysts of interest in this work are defined as those only mono-N-substituted, with a chloride counter ion, and a substituent group which has the DABCO molecule bound in the β-position, as with CM-DABCO. Within these definitions, a range of structures have been synthesised previously, featuring both polar and non-polar groups, including the linkage together of two DABCO molecules.

6 Selection of Catalyst and Substrate Structures

In the selection of the catalyst structures to use within this work, there are several considerations to make on top of the criteria presented in Section 4.2, which narrowed the structures of interest to those mono-N-substituted, with chloride counter ion and with DABCO in the β-position to the derivative functional group. These additional considerations will be talked about within this section, before the selection of the structures to be tested are presented. Discussed also are the organic substrates that the reactions of HOCl will be tested with in the kinetic studies. Further information about the conditions of the kinetic studies is found in Section 8.4.

6.1 Catalyst Structures

The first of the additional selection factors is within the catalyst synthesis itself – with favour given to those structures that have been previously synthesized, and are performed in one step with simple work-up. Thus for example, routes that involve follow-up reduction or oxidation reactions are less optimal, or those requiring complicated techniques that add difficulty to any potential scale-up.

As in Section 2.5, the pKa of the catalyst is also important to consider, with catalytic activity decreasing as the pH is moved away from catalyst pKa. Hence, if the pKa is too high or low, the catalyst is likely to be of lower efficiency at pH values between 3 and 6, which is the region of interest particularly in the H_{cat} and D_{cat} pulping stages[17–19,34].

DABCO has two pKa values, at 8.82 and 2.97.[78] The derivative group likely mimics the effect this first protonation has, with both mono-protonated DABCO and each DABCO-derivative having a positive charge. The base point for the expected pKa of the DABCO-derivatives can then be considered as being around 2.97.

It is hypothesised here that there are two main effects that the functional group within the derivative will have on this pKa. Firstly is the involvement of a hydrogen-bond donor. In its mono-protonated state, it is possible that DABCO is capable of forming extensive hydrogen-bond networks, which would have the effect of stabilising this catalyst form, lowering the pKa of the second amine group, as has been reported in other compounds[98].

Thus the use of a hydrogen-bond donor within the derivative could have a similar impact. Amides, amines and hydroxyl groups are all capable of hydrogen bond donating, with varying strengths (amine < alcohol < amide), and so the use of these could help ensure a low catalyst pKa[99].

The second change the functional group could cause to the catalyst pKa is a result of the inductive effect from having a strongly electron withdrawing or donating group bound to the DABCO molecule. These could have the effect of respectively either decreasing or increasing the nucleophilicity of the amine lone pair, which would have a knock-on effect on the pKa of the amine, as well the catalyst activity itself.

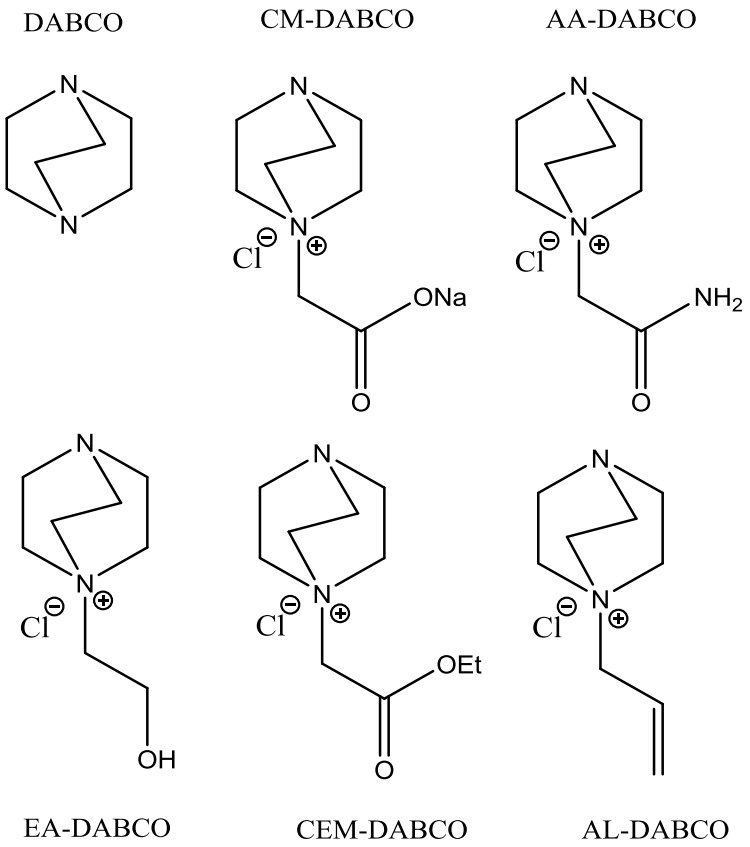


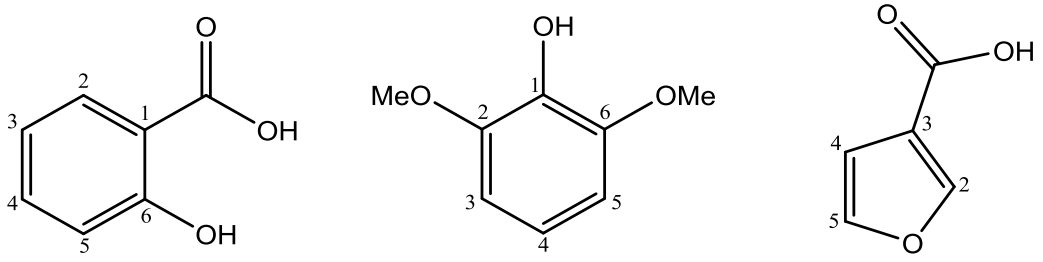
Figure 17: The catalyst structures selected to be tested.

The selected catalysts then cover a range of functional group types, as shown in Figure 17. AA-DABCO and EA-DABCO both feature hydrogen-bond donating groups in an amide and alcohol respectively. An amine group was not selected due to only being synthesized previously with a bromide counter-ion in low yield[91]. CEM-DABCO has a polar ester group that is not capable of hydrogen-bond donating, whilst AL-DABCO has a non-polar allyl group. Finally, DABCO and CM-DABCO are to be tested, to provide comparison and relevance to these results compared to catalysts used in H_{cat} pulp bleaching stages previously. CEM-, CM- and AA-DABCO also provide indication of the inductive effect of the functional group discussed above.

6.2 Substrate Structures

The first selected model compound to be tested is salicylic acid. Within plant cells, salicylic acid performs many uses including defence, growth and signal mediating[100]. This is chosen due to research being previously performed on the reaction kinetics between this and HOCl, including with tertiary amine catalysts, with reaction rates reported.[16,35] Additionally, it has been reported that following reaction with HOCl, a significant UV shifts occurs, with a red-shift from the formation of both 3- and 5-chlorosalicylic acid[35].

Salicylic acid however is a poor model for lignin, due to it having a phenol pKa of 13.4, higher than those found in lignin[51]. In order for close comparison to bleaching studies then, syringol was also selected to be tested. This acts as a closer model compound for lignin, the removal of which forms a large part of the bleaching process. Syringol is expected to be chlorinated and oxidized into a range of aromatic and



Salicylic Acid
pKa = 2.97, 13.40

Syringol
pKa = 9.98

3-Furoic Acid
pKa = 3.90

Figure 18: The structures of the organic substrates to be used in the kinetic studies.

quinonic structures, in the same way lignin is during the bleaching process, rather than simply being mono-chlorinated as with salicylic acid[50].

The final tested aromatic substrate is 3-furoic acid. This bears a similar structure to HexA, and thus again provides some indication of the effect on pulp bleaching of each catalyst, although major differences are expected due to its aromaticity, which is not the case in HexA. Electrophilic substitution reactions, as with the other aromatic groups, are dominant, rather than the addition that takes place in HexA.[101] The main expected reaction takes place at the 5-position, with this having the most stabilised intermediate. It can then be expected to react similarly to salicylic acid, with direct electrophilic chlorination, with more complexity possible as this reaction is less studied. The structures of the tested substrates are shown in Figure 18.

7 Results and Discussion

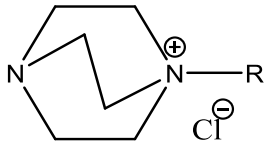
7.1 Catalyst Synthesis

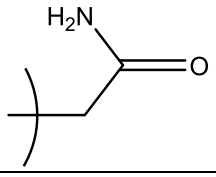
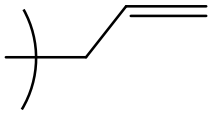
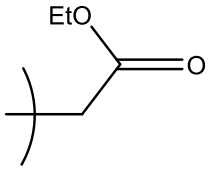
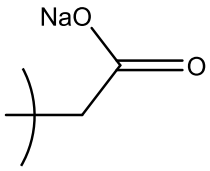
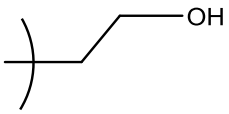
The synthesis procedures for the DABCO-derivative catalysts can be found in Section 8.2. ^{1}H and ^{13}C NMR are within Appendices 1-5.

Table 1 shows the yields obtained from the synthesis of each catalyst. It can be seen that although generally high yields and purities could be achieved, the yield for EA-DABCO was low, at around 17%. This is unexpected from literature[26], and a possible cause is the washing solvents used not being anhydrous, causing a loss of product due to it having a high water solubility. The white solid produced was also very fine, meaning losses during the filtration are probable.

When the equivalence of DABCO to organochloride is also considered, there is a large amount of DABCO being wasted in these reactions, with as low as 0.2 equivalences being utilised (hence 0.8 equivalence of DABCO is wasted). Testing could also be undertaken to see if these equivalences can be increased, if it is seen that this does not come with a notable decrease in product purity. On a larger scale, DABCO could also potentially be recycled between reactions, reducing waste.

Table 1: The conditions and yields produced of the synthesis of the tested catalyst structures.



Catalyst Name	R Group	Organochloride Equivalence	Reaction Time (hrs)	Yield (%)
AA-DABCO		0.93	20	64
AL-DABCO		0.5	24	75
CEM-DABCO		1	1	75
CM-DABCO		N/A‡	1	95 (71)‡‡
EA-DABCO		0.2	48	17

‡ CM-DABCO was synthesised from CEM-DABCO so did not feature an organohalide.

‡‡ Yield including the synthesis of CEM-DABCO.

Another factor to be improved in these reactions are the reaction times. In most cases, reaction times of over 20 hours were involved in the syntheses, which in many instances is likely unnecessary. This can be seen from the synthesis of CEM-DABCO, which utilises only a 1 hour reaction time, and still produces yields of over 70%. Optimisation of the reaction conditions, particularly reaction time, is therefore required before any production of the catalysts on a larger scale.

Something else that should be considered with regard to these reaction routes are the safety and environmental aspects. 2-chloroethanol, as used in the synthesis of EA-DABCO, as well as allyl chloride, used in AL-DABCO, are both highly toxic reagents, and as such on a larger scale these catalysts are less favourable to produce. Comparatively, CEM, CM and AA-DABCO all involve the use of far less toxic

organochlorides in ethyl chloroacetate and 2-chloroacetamide, and hence are preferable to use.

In terms of synthesis complexity, CM-DABCO is the only catalyst to require two synthesis steps, compared to one step in all other cases. This makes CEM- and AA-DABCO the optimal choices from a synthesis and scale-up viewpoint, assuming they do not feature vastly inferior catalytic abilities.

7.2 Catalyst pKa Measurements

Shown in Table 2 are the measured pKa values of each of the utilised catalysts. The titration curves used to obtain these values can be found in Appendix 6.

Table 2: The experimentally calculated pKa values of the tertiary amine catalysts.

Catalyst Name	pKa_1	pKa_2
DABCO	2.97*	8.82*
AA-DABCO	3.0	-
AL-DABCO	3.2	-
CEM-DABCO	3.1	8.0
CM-DABCO	3.4	-
EA-DABCO	3.4	9.0
*Literature values, not tested in this work.		

In all cases, the pKa of the tertiary amine is similar to, and slightly higher than, that of the second amine of DABCO. This shows that the hypothesis presented earlier, that the derivative group featuring a hydrogen-bond donor has a pKa lowering effect, is likely incorrect, as AL-DABCO and CEM-DABCO have similar pKa values to those with these groups. The second part of the hypothesis, relating to the inductive effect of the groups, has some evidence to support it, with the order of CM->CEM->AA-DABCO being the same as the relative electron withdrawing ability of these groups.

Both CEM-DABCO and EA-DABCO appeared to also have a second equivalence point, and hence a second pKa value. In the case of CEM-DABCO, there is expected to be no pKa in this region, meaning the compound is reacting during addition of NaOH. This reaction is the hydrolysis of the ester group to form CM-DABCO, which consumes hydroxide ions and results in an unstable pH, as is evident in Appendix 6c.

The second pKa is therefore just the point where this reaction no longer occurs, causing a sharp pH rise.

For EA-DABCO, it is unlikely that the alcohol group has a pKa as low as 9.0, so it is more probable that a degradation or other further reaction is happening here also. The increase surrounding the equivalence point is also not sharp, meaning this could also not be showing a second pKa value. Like CEM-DABCO, approximately double the NaOH volume is needed for EA-DABCO than for the other tested catalysts, which could suggest either an NaOH consuming reaction, or a buffering effect coming from the presence of a pKa.

The relatively low difference in the amine pKa values of all the catalysts suggests that there may be a relatively minor difference in the activities of the catalysts, as will now be investigated within kinetic studies.

7.3 Kinetic Studies

7.3.1 Reaction with Salicylic Acid

The chlorination of salicylic acid results in an increase in absorption above 300 nm, and a decrease of the peak found at 298 nm, as shown in Figure 19. Hence a red-shift of the peak occurs, as is expected from literature during the formation of 3- and 5-chlorosalicylic acid[16]. The wavelength that is followed is thus selected as 324 nm.

Table 3 and Figure 20 display the maximum gradient and the catalytic factors obtained at pH 3, 5 and 7 with the tested catalysts. The catalytic factor relates to the ratio of the

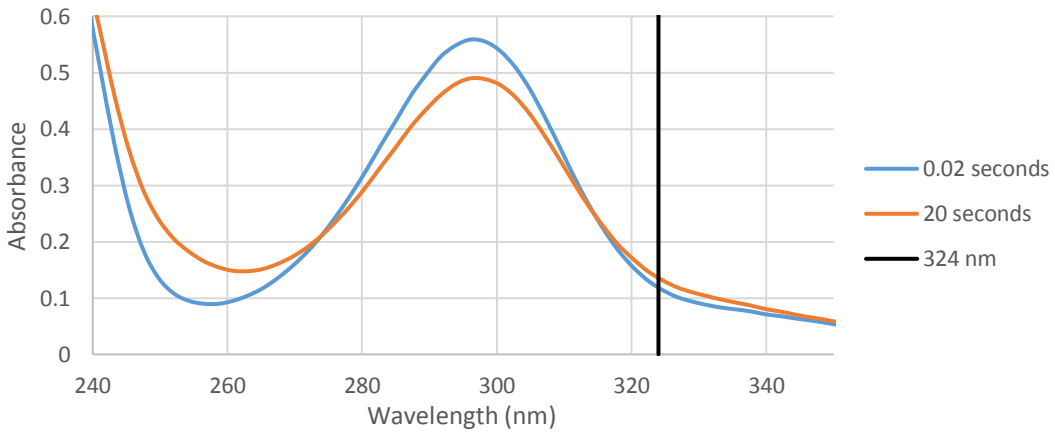


Figure 19: The change in the UV-spectrum of salicylic acid following reaction with HOCl.

Table 3: The impact of tertiary amine catalysts on the rate of the reaction between HOCl and salicylic acid.

	pH 3		pH 5		pH 7	
Catalyst	**Gradient (s^{-1})**	**Catalytic Factor**	**Gradient (s^{-1})**	**Catalytic Factor**	**Gradient (s^{-1})**	**Catalytic Factor**
None	0.1043 ± 0.0029	**1.00 ± 0.04**	0.0034 ± 0.0002	**1.00 ± 0.08**	0.0078 ± 0.0001	**1.00 ± 0.03**
DABCO	0.2386 ± 0.0091	**2.29 ± 0.07**	0.0513 ± 0.0015	**15.20 ± 0.91**	0.0572 ± 0.0003	**7.34 ± 0.13**
AA-DABCO	0.2591 ± 0.0059	**2.48 ± 0.07**	0.0314 ± 0.0024	**9.29 ± 0.56**	0.0081 ± 0.0003	**1.04 ± 0.04**
AL-DABCO	0.2729 ± 0.0066	**2.62 ± 0.08**	0.034 ± 0.0006	**10.08 ± 0.60**	0.0073 ± 0.0006	**0.93 ± 0.09**
CEM-DABCO	0.2699 ± 0.0153	**2.59 ± 0.09**	0.0327 ± 0.0006	**9.69 ± 0.58**	0.0083 ± 0.0009	**1.07 ± 0.11**
CM-DABCO	0.2541 ± 0.0117	**2.44 ± 0.08**	0.0482 ± 0.0008	**14.30 ± 0.86**	0.0088 ± 0.0008	**1.13 ± 0.10**
EA-DABCO	0.2831 ± 0.0028	**2.71 ± 0.08**	0.0377 ± 0.0013	**11.17 ± 0.67**	0.0083 ± 0.0003	**1.07 ± 0.04**

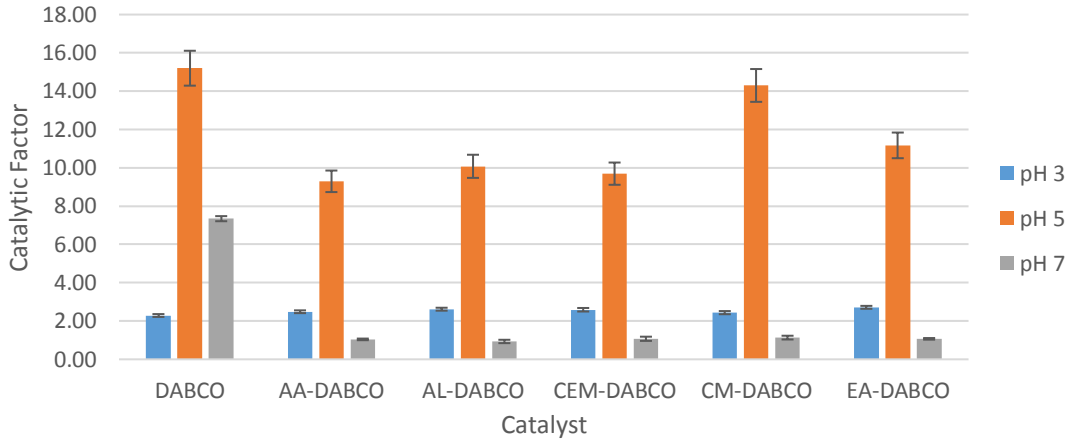


Figure 20: The catalytic factors of the tertiary amine catalysts in the reaction of HOCl and salicylic acid.

maximum gradients of the catalyzed and uncatalyzed reactions, as shown in Equation 8 in Section 8.4.

Considering first the uncatalyzed rates, pH 3 has a far higher rate than either pH 5 or pH 7, likely due to the presence of Cl_2 also performing the chlorination reaction at pH 3[39,67]. The rate at pH 7 is then also around twice that of pH 5, with the probable cause of this being the use of phosphate buffer at pH 7 only, which is known to also have a catalytic effect on HOCl reactions[35].

Moving then onto considering the catalytic effect at each pH value, at pH 3 each of the tested structures has a catalytic factor of between around 2.3 and 2.7. Hence, they are not only very close to each other, they also all catalyse a relatively small amount. This

is partially for the same reason as above, the Cl_2 chlorination occurring, but is also a result of the dominant form of each of the catalysts being the protonated form at pH 3, which is known to be the less active form[18].

It can be seen however at pH 5 that the structure of the catalyst is having a far larger impact. Here, the catalytic factors are higher, with DABCO the highest at 15.20, and there is a substantial difference between the catalysts, with AA-DABCO the lowest at 9.29. Of the derivative structures, CM-DABCO has the highest factor, only slightly lower than DABCO, with EA-DABCO the next highest. This shows a correlation with the catalyst pKa values, with CM-DABCO and EA-DABCO having the highest, and hence the closest to pH 5, as will be investigated in more depth in Section 7.3.4.

At pH 7, with the exception of DABCO, all the structures produce no strong evidence of catalysing the reaction, with catalytic factors close to 1. This is an expected result considering the difference in pH between this and the catalyst pKa values of close to 3. DABCO, with a pKa also of 8.87, catalyses by a factor of around 7. The catalytic effect of the phosphate buffer in use also likely lowers the tertiary amine catalytic factors[35].

It can be concluded from salicylic acid then that at both pH 3 and 7, the DABCO-derivatives poorly catalyse the reaction, and the differences caused the derivative functional group are minor. Comparatively, pH 5 produces high rates of catalysis in all cases, as this pH corresponds the best of those tested to the catalyst pKa values. It also appears from these results that CM-DABCO catalyses the highest amount of any of the derivatives at pH 5.

It is important however that before making final conclusions, this is tested with the other substrates to see if similar results are found.

7.3.2 Reaction with 3-Furoic Acid

Like with salicylic acid, the reaction of 3-furoic acid with HOCl involves a red-shift of the UV-spectrum, with above 250 nm increasing as reaction occurs, as seen in Figure 21. This is likely a result of the chlorination at the most reactive 5- position of the furan ring, which is an electrophilic substitution reaction[101]. Here, 265 nm was selected as the monitored wavelength.

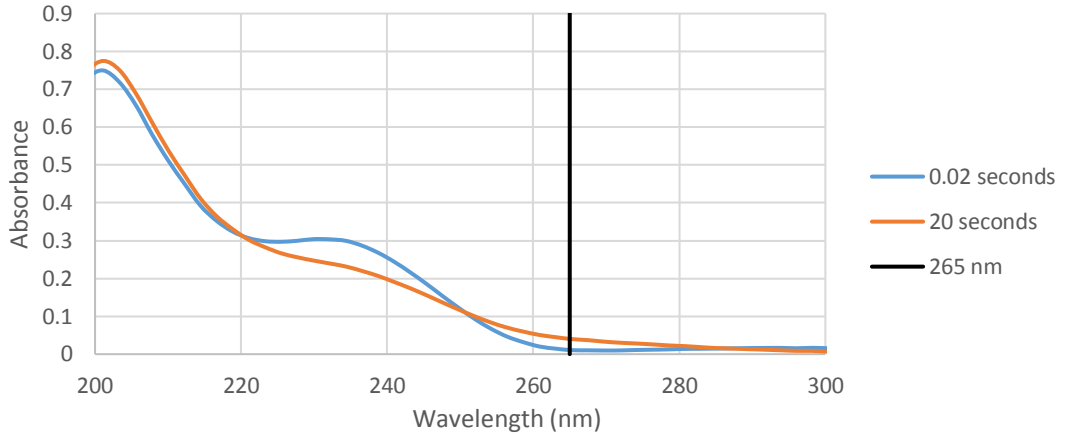


Figure 21: The change in the UV-spectrum of 3-furoic acid following reaction with HOCl.

The maximum gradients and catalytic factors of the reactions with 3-furoic acid are shown in Table 4 and Figure 22. Like with salicylic acid, when uncatalyzed the pH 3 reaction is far faster than either pH 7 or pH 5, although the difference here is smaller. The catalytic effect of the phosphate buffer again results in an increased rate at pH 7 compared to pH 5[35], although this is also smaller than for 3-furoic acid.

In terms of the catalytic ability, starting with pH 3, the factors are now higher than they were for salicylic acid, and the catalyst structure also seems to have slightly more of an effect, with CM-DABCO and EA-DABCO the highest, and DABCO the lowest. CM-DABCO and EA-DABCO being higher is unexpected based off of pKa alone, as these have the pKa the furthest away from 3.

Like with salicylic acid, it is again pH 5 which has the greatest difference between the derivatives, and also has CM-DABCO as the most active, followed by EA-DABCO. The catalytic factors are however in all cases lower than with salicylic acid, the highest being 5.24.

When comparing to salicylic acid, both the lowered difference between pH 3 and 5 reactions, as well as the increased catalytic factors at pH 3, can be justified by the nucleophilicity of the substrate. As discussed by Silvey et al., the importance of Cl_2 and Cl_2O in the chlorination reaction decreases as substrate nucleophilicity is increased, as can be assumed is the case here with 3-furoic acid compared to salicylic acid.[2] It is then the case that HOCl, and therefore the chlorammonium cation, is doing a larger amount of the chlorination at pH 3 in 3-furoic acid, resulting in higher catalytic factors and closer results between pH values of 3 and 5.

Table 4: The impact of tertiary amine catalysts on the rate of the reaction between HOCl and 3-furoic acid.

	pH 3		pH 5		pH 7	
Catalyst	**Gradient (s^{-1})**	**Catalytic Factor**	**Gradient (s^{-1})**	**Catalytic Factor**	**Gradient (s^{-1})**	**Catalytic Factor**
None	0.0417 ± 0.0009	**1.00 ± 0.03**	0.0041 ± 0.0007	**1.00 ± 0.24**	0.0166 ± 0.0004	**1.00 ± 0.03**
DABCO	0.0882 ± 0.0018	**2.12 ± 0.05**	0.0143 ± 0.0002	**3.47 ± 0.60**	0.0021 ± 0.0005	**0.13 ± 0.24**
AA-DABCO	0.1540 ± 0.0017	**3.69 ± 0.08**	0.0114 ± 0.0001	**2.76 ± 0.48**	0.0167 ± 0.0003	**1.01 ± 0.03**
AL-DABCO	0.1609 ± 0.0017	**3.86 ± 0.09**	0.0127 ± 0.0002	**3.10 ± 0.53**	0.0156 ± 0.0008	**0.94 ± 0.05**
CEM-DABCO	0.1435 ± 0.0008	**3.44 ± 0.08**	0.0118 ± 0.0001	**2.87 ± 0.50**	0.0165 ± 0.0001	**0.99 ± 0.02**
CM-DABCO	0.1758 ± 0.003	**4.22 ± 0.09**	0.0216 ± 0.0003	**5.24 ± 0.90**	0.0166 ± 0.0003	**1.00 ± 0.03**
EA-DABCO	0.1755 ± 0.0041	**4.21 ± 0.10**	0.0157 ± 0.0001	**3.83 ± 0.66**	0.0157 ± 0.0003	**0.95 ± 0.03**

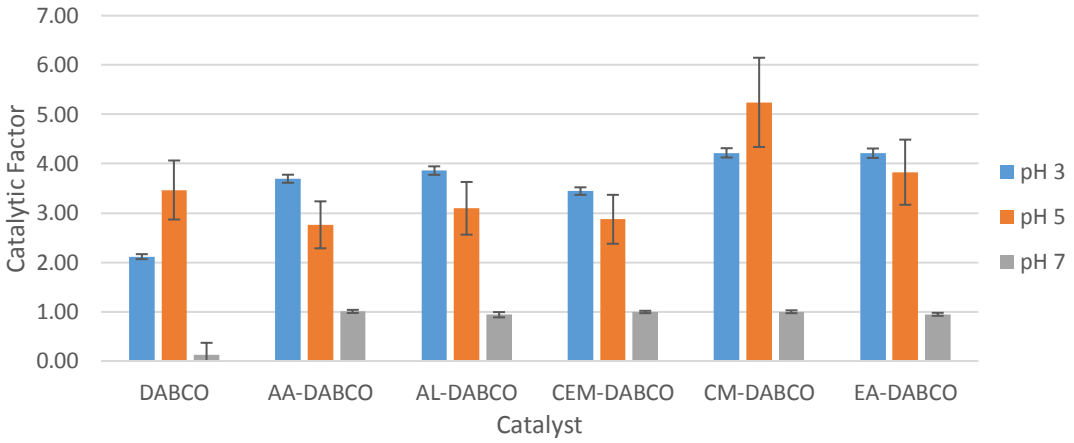


Figure 22: The catalytic factors of the tertiary amine catalysts in the reaction of HOCl and 3-furoic acid.

A hypothesis for the lowered pH 5 catalytic factors also relates to this higher substrate nucleophilicity. As the uncatalyzed reaction is happening more rapidly as a result of this, the relative effect of the catalyst is lowered. A less reactive substrate, such as salicylic acid, has a slower uncatalyzed reaction and therefore a greater activity of the catalyst is seen.

As expected, the catalytic factors at pH 7 display the DABCO-derivatives do not catalyse the reaction, or catalyse it only slightly, as with salicylic acid. The cause of the low catalytic factor listed for DABCO is an inhibition time before gradient increase, as can be seen in Figure 23. The cause of this is unknown, but does display the interesting effects that the structure of the tertiary amine can have.

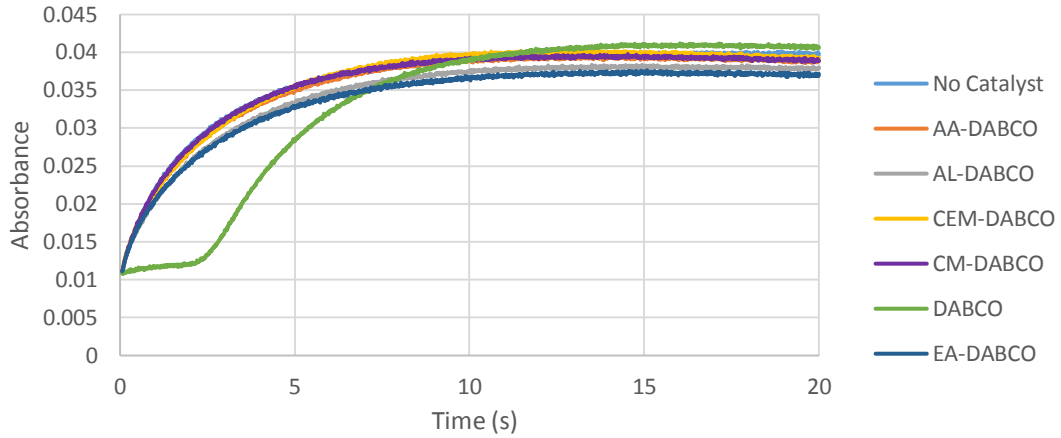


Figure 23: The change in absorbance at 265 nm following the reaction of 3-furoic acid and HOCl at pH 7.

Overall, 3-furoic acid displays some of the same conclusions as with salicylic acid, with catalysis being evident at pH 5, especially in the case of CM-DABCO. The order also again corresponds well to the pKa values of the catalyst found earlier. There are however additional conclusions, relating to the nucleophilicity of the substrate, with a more nucleophilic substrate seeming to both produce improved catalytic factors at pH 3, as well as decreased ones at higher pH values. The catalyst structure can also result in unexpected deviations from simple reaction orders, as shown in Figure 23.

7.3.3 Reaction with Syringol

Syringol behaves differently to salicylic acid and 3-furoic acid. Shown in Figure 24 is the change in the UV-spectrum of syringol upon reaction with HOCl. Dissimilarly to both salicylic acid and 3-furoic acid, when reacted with HOCl, syringol is oxidized into a variety of coloured products, as with lignin in pulp bleaching, and hence there is an absorbance increase across the entire spectrum[50]. Particularly increased is the

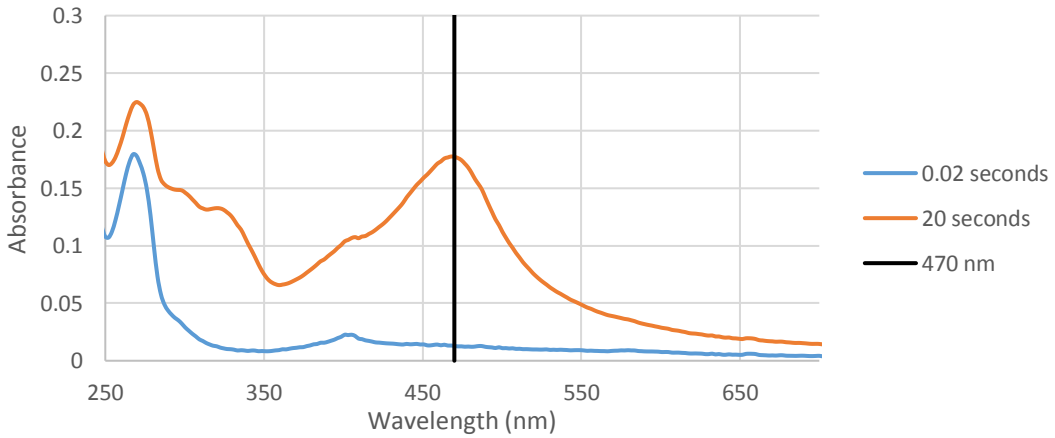


Figure 24: The change in the UV-spectrum of syringol following reaction with HOCl.

Table 5: The impact of tertiary amine catalysts on the rate of the reaction between HOCl and syringol.

	3		5		7	
Catalyst	**Gradient (s^{-1})**	**Catalytic Factor**	**Gradient (s^{-1})**	**Catalytic Factor**	**Gradient (s^{-1})**	**Catalytic Factor**
None	0.131 ± 0.0006	**1.00 ± 0.01**	0.0769 ± 0.0012	**1.00 ± 0.02**	0.102 ± 0.0031	**1.00 ± 0.04**
DABCO	0.1864 ± 0.0019	**1.42 ± 0.01**	0.4604 ± 0.001	**5.99 ± 0.09**	0.6295 ± 0.0006	**6.17 ± 0.18**
AA-DABCO	0.2105 ± 0.0017	**1.61 ± 0.01**	0.1479 ± 0.001	**1.92 ± 0.03**	0.1908 ± 0.0005	**1.87 ± 0.06**
AL-DABCO	0.1896 ± 0.0037	**1.45 ± 0.02**	0.1554 ± 0.0022	**2.02 ± 0.03**	0.2078 ± 0.0014	**2.04 ± 0.06**
CEM-DABCO	0.2015 ± 0.0014	**1.54 ± 0.01**	0.1651 ± 0.0023	**2.15 ± 0.04**	0.2661 ± 0.0013	**2.61 ± 0.08**
CM-DABCO	0.1762 ± 0.0015	**1.34 ± 0.01**	0.1806 ± 0.0025	**2.35 ± 0.04**	0.2548 ± 0.0011	**2.50 ± 0.07**
EA-DABCO	0.193 ± 0.0027	**1.47 ± 0.02**	0.1735 ± 0.0022	**2.26 ± 0.04**	0.2248 ± 0.0029	**2.20 ± 0.07**

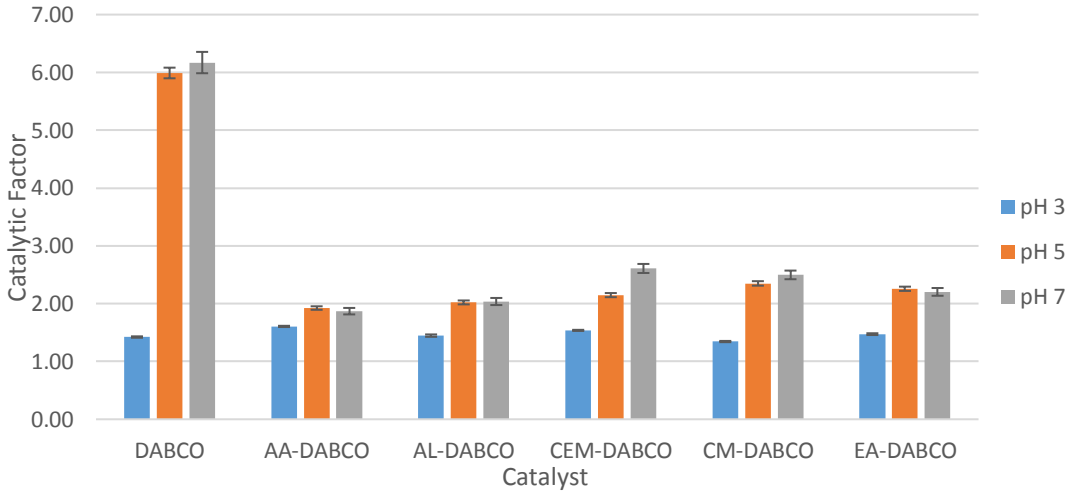


Figure 25: The catalytic factors of the tertiary amine catalysts in the reaction of HOCl and syringol.

wavelength range between around 420 nm and 520 nm, the maximum of which is found at 470 nm, and thus this is the wavelength used to monitor the reactions.

Table 5 and Figure 25 show the maximum gradients and catalytic factors within the experiments of syringol. Overall, there are many differences between syringol and the other two substrates. In regards to the uncatalyzed reactions, the gradients are far closer here, with the rate at pH 3 only double that of pH 5, and less than double the rate at pH 7.

The next major difference is in the catalytic factors, which are very low for the DABCO-derivatives at all pH values tested, which is especially different when

considering pH 5. Here, DABCO has a factor significantly higher than its derivatives, as it does at pH 7. Additionally, the factors at pH 7 are actually higher than at lower pH values, unlike in salicylic acid and 3-furoic acid where the derivatives had almost no effect on the rate.

This together displays the major impact that the substrate structure has on the reaction. Syringol, as a phenol with no carboxylic acid group, has a pKa of 9.98, compared to the far more acidic pKa values of the other two substrates. It also reacts very differently, producing a range of conjugated and quinonic products, and hence is a more complex system than in the other cases.

As such, it is possible that the reaction between syringol and HOCl or the chlorammonium cation is not the one being monitored by the absorbance increase at 470 nm. If this reaction is far faster than a subsequent absorbance increasing reaction, the apparent effect of the catalyst would be far lower, as only a small fraction of the overall increase is a result of the catalyzed reaction.

An alternative possibility is that that some of the further reactions that reduce absorbance also involve HOCl, in which case these would also be catalysed. This would again result in a lower effective catalytic factor being obtained, as the observed effect would be of the difference between the two catalysed reactions. Reactions that decrease the absorbance can be seen to happen from the graphs found in Appendix 10, which show a decrease in absorbance between the peak and the end of the monitored time period.

Overall however this displays the advantage of the use of substrates with a more simple reaction pathway, such as simple chlorination reactions as with salicylic acid. It also shows again that the substrate is a major factor in the reactions of HOCl, and therefore results should be considered carefully with the structure of the substrate in mind.

7.3.4 Results at pH 5

Of the pH values tested, it is pH 5 that has the most relevance in H_{cat} pulp bleaching stages[17–19,34,59]. This has also been the pH that has shown in this work to be the most affected by the structure of the catalyst, particularly for salicylic acid. As such, the catalytic factors for pH 5 between the three substrates are shown in Table 6. This

comparison also allows for a better observation of the effect of the substrate on the kinetic results.

Table 6: The pKa values of each DABCO-derivative and their catalytic factors at pH 5.

			Salicylic Acid		3-Furoic Acid		Syringol	
Catalyst	pKa	Order‡	Catalytic Factor	Order‡	Catalytic Factor	Order‡	Catalytic Factor	Order‡
CM-DABCO	3.4	1	14.30 ± 0.86	1	5.24 ± 0.90	1	2.35 ± 0.04	1
EA-DABCO	3.4	1	11.17 ± 0.67	2	3.83 ± 0.66	2	2.26 ± 0.04	2
AL-DABCO	3.2	3	10.08 ± 0.60	3	3.10 ± 0.53	3	2.02 ± 0.03	4
CEM-DABCO	3.1	4	9.69 ± 0.58	4	2.87 ± 0.50	4	2.15 ± 0.04	3
AA-DABCO	3.0	5	9.29 ± 0.56	5	2.76 ± 0.48	5	1.92 ± 0.03	5
‡ Order from the highest to lowest.								

Due to CM-DABCO already having been shown to provide more efficient bleaching than DABCO, as a result of DABCO's instability in HOCl, only the DABCO-derivatives are now considered[19,34,54]. The existence of the second pKa of DABCO also makes the results featuring it more complex to analyse, as the closeness to both has to be considered.

For all three substrates it can be seen that the order of the DABCO-derivative catalyst activities is very similar, with an identical order between salicylic acid and 3-furoic acid. Hence the substrate structure impacts the overall catalytic factors, but it appears selectivity between the catalysts to different structures is not a factor to consider.

CM-DABCO in each case has the highest activity, followed by EA-DABCO. For syringol, CEM-DABCO in the next most active, followed by AL-DABCO, whilst for the others AL-DABCO is the more active of the two. AA-DABCO is the least active catalyst in all cases.

These orders fit well also with the calculated pKa values of the catalysts, shown also in Table 3, with EA-DABCO and CM-DABCO having the highest pKa, followed by AL-, CEM- and AA-DABCO. This order is identical to that obtained for salicylic acid and 3-furoic acid activities, with the only deviation being the difference between CM- and EA-DABCO. Hence it can be preliminarily said that the activity of the catalyst is

directly increased by moving the pKa closer to the experimental pH, or lowering experimental pH to the catalyst pKa. Additionally, the structure of the substrate impacts the catalytic factors, but not the catalyst selectivity.

It should be noted however that the large relative errors within the salicylic acid and 3-furoic acid results mean these orders are not definitive, with catalysts often falling within error of each other, particularly with 3-furoic acid. The pKa measurements were also only performed once, meaning the error within these is unknown. In Section 8.3.6 can be found additional discussion of other sources of error. Overall, further testing to improve reliability is needed. This conclusion also fits poorly the pH 3 and 7 results, shown in Appendix 7, showing the situation is more complex than concluded.

7.3.5 Catalyst Stability

As discussed within the literature review of this work, many tertiary amines are prone to degradation within the HOCl reaction medium[16,54]. This includes DABCO, as has been concluded from H_{cat} bleaching studies and previously[18,54]. Hence, despite a higher rate of reaction catalysis in some cases, it is likely that DABCO also degrades far more rapidly than other catalysts. It is then of interest to observe the difference in stabilities between the other catalysts, as well as of DABCO itself.

The stability of each of the catalyst structures was studied via the use of delays, with the catalysts pre-incubated with HOCl for a delay time before organic substrate addition. Figure 26 displays the effect of delay time on each of the catalysts, with the

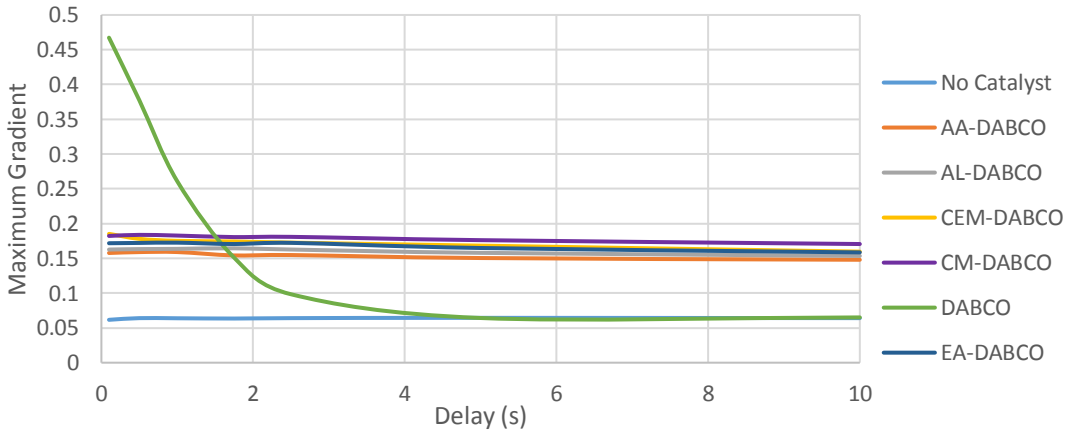


Figure 26: The effect of the length of pre-incubation time of DABCO-based catalysts and HOCl on their reaction with syringol at pH 5.

substrate used being syringol at pH 5. The results from pH 3 and 7 can be found in Appendix 11, with relatively similar results obtained.

As can been seen, DABCO undergoes first order degradation, and has completely degraded in around 4 seconds, with the rate very similar to the no catalyst result from then. Each of the DABCO derivatives appear to be fully stable up to at least 10 seconds of pre-incubation, with only a small decrease in activity seen in all cases.

It is good to note however that this does not necessarily show that DABCO will degrade rapidly when used in pulping or similar systems. When another substance is present, the degradation depends on the balance of rates between the possible reactants, as if both the chlorammonium cation and subsequent substrate chlorination are far faster than the degradation reaction between DABCO and HOCl, this reaction will only occur in small amounts until the substrate is consumed. It would however make recycling difficult, as degradation would occur as soon as no substrate is present.

One other way of considering these results in the difference in gradient between certain delay times and the first delay time of 0.1 s. In Table 7 is shown this ratio for 2.5 s, for each pH value. 2.5 s was selected to be discussed as it is the last point before complete DABCO degradation, as shown in Figure 25, so should give the best idea of differences in the rates of degradation. Appendix 12 displays equivalent tables for pH 3 and 7.

Table 7: The effect of 2.5s HOCl and catalyst pre-incubation time on their reaction with syringol.

	Gradient at 2.5 s delay compared to 0.1 s		
Catalyst	**pH 3**	**pH 5**	**pH 7**
None	0.97 ± 0.02	1.04 ± 0.04	0.91 ± 0.02
DABCO	**0.70 ± 0.01**	**0.21 ± 0.01**	**0.16 ± 0.01**
AA-DABCO	1.01 ± 0.01	0.98 ± 0.02	1.01 ± 0.02
AL-DABCO	0.92 ± 0.04	1.00 ± 0.04	0.99 ± 0.05
CEM-DABCO	1.01 ± 0.02	0.93 ± 0.02	0.99 ± 0.02
CM-DABCO	0.92 ± 0.03	0.99 ± 0.02	1.01 ± 0.03
EA-DABCO	1.05 ± 0.08	1.00 ± 0.09	0.96 ± 0.1

As expected, DABCO is the only catalyst to undergo substantial degradation within this time, with a loss of 84% in the gradient at pH 7 and 79% at pH 5. It appears more stable at pH 3, but this can also be the result of the reaction occurring without utilising the catalyst, meaning a much smaller decrease is seen despite possible similar levels of degradation.

There are some small differences between the degradation of the DABCO-derivative catalysts. In all pH values tested, AA-DABCO is fully stable, with no loss of activity seen. Both AL-DABCO and CM-DABCO are fully stable at pH 5 and 7, but suffer some possible degradation at pH 3. These are in contrast to CEM-DABCO and EA-DABCO, which have small amounts of degradation at pH 5 and pH 7 respectively.

The small nature of these differences however does make them prone to error, particularly in EA-DABCO, where the standard deviation is higher. Without further runs then, these differences should not be considered too strongly, and it can overall be said that all of the DABCO-derivatives are close to fully stable for up to 10 seconds of reaction.

7.3.6 Discussion of Errors

Within the kinetic measurements taken within this report, there are a number of different errors to consider. Although all experiments were performed in triplets, improving reliability, some errors also fall outside of the report standard deviations that are found from these.

One of the main errors relates to the preparation of the catalyst samples themselves. Due to the catalysts being hydroscopic, they absorb water readily. This means that high levels of accuracy in the measurement of yields can be difficult, as can be the preparation of solutions. Even small differences in the water amount in the solid catalyst has a large effect on the solutions once diluted down. As there was a limited amount of solid catalysts, many experiments were run using the same initial prepared solutions, and hence errors may not be represented in the standard deviations shown when repeats were from the same initial solution.

Another reliability issue relates to the stopped-flow spectrometer itself. Through the laboratory work, many issues with the machine were found that could have impacted result accuracy. This includes large baselines shifts between catalyst runs and the input lead for the UV light becoming loosened easily, causing a fluctuating absorbance line. Whilst these errors were attempted to be minimised and accounted for, some error from them is likely still present, and this is the most probable cause of the some of the larger standard deviations found within this work.

8 Materials and Methods

8.1 Raw Materials

All reagents used within this thesis work were purchased in high purity from suppliers and used as received.

Chemicals used for catalyst syntheses included DABCO, 2-chloroacetamide, ethyl chloroacetate, 2-chloroethanol, allyl chloride and sodium hydroxide pellets. Solvents utilised were ethyl acetate, acetonitrile and distilled water. ^{1}H and ^{13}C NMR studies of the catalysts used deuterated water (D_2O). HCl solutions used in the pKa titrations were prepared from a stock 37% HCl solution, whilst NaOH solutions were prepared using NaOH pellets dissolved in water and subsequently diluted to the desired concentration.

Organic substrates utilised within kinetic studies were salicylic acid, syringol and 3-furoic acid. The concentration of NaOCl was determined on the same day as experiments via iodometric titration as described in the standard method SCAN-C 29:72.

Commercial citrate buffers of both pH 3 and pH 5 were purchased from suppliers. The pH 7 phosphate buffer was prepared from H_3PO_4 and NaOH in water, prior to dilution.

8.2 Synthesis of Catalyst Structures

^{1}H and ^{13C} NMR spectra were obtained using a Bruker AVANCE III 400 MHz 5 mm (BBFO) NMR spectrometer, and analysed using TopSpin 3.0 software from Bruker. The ^{1}H and ^{13}C NMR spectra can be found in Appendices 1-5.

Synthesis of AA-DABCO: AA-DABCO was synthesised using modifications to a literature reaction[82]. A solution of 2-chloroacetamide (1.112 g, 11.89 mmol) in 25 mL ethyl acetate was added to DABCO (1.440 g, 12.84 mmol) in 25 mL ethyl acetate at 0°C. The reaction was then left stirring at room temperature for 20 hours, before the resulting precipitates were collected, washed with ethyl acetate (3x30mL) and dried under vacuum to give AA-DABCO as a white solid (1.496 g, 64%). ^{1}H NMR (400

MHz, D_2O): δ_H 3.14 (6H, t, $^3J_{HH}$ = 7.6, $(CH_2)_3N^+$), 3.58 (6H, t, $^3J_{HH}$ =7.6, $(CH_2)_3N$), 3.98 (2H, s, $N^+\underline{CH_2}CONH_2$). ^{13}C NMR (400 MHz, D_2O): δ_C 44.05, 53.03, 62.57, 166.10.

Synthesis of AL-DABCO: AL-DABCO was synthesised using modifications to a literature reaction[29]. DABCO (3.213 g, 28.64 mmol) was dissolved in 25 mL ethyl acetate, before allyl chloride (1.17 mL, 14.32 mmol) was added dropwise to the stirred solution and the reaction was left for 24 hours. The resulting white precipitate was washed with ethyl acetate (3x30 mL) and diethyl ether (3x30mL) and dried under vacuum to give AL-DABCO as a white solid (2.04g, 75%). ^1H NMR (400 MHz, D_2O): δ_H 3.09 (6H, t, $^3J_{HH}$ = 7.9, $(CH_2)_3N^+$), 3.32 (6H, t, $^3J_{HH}$ = 7.9, $(CH_2)_3N$), 3.80 (2H, d, $^3J_{HH}$ =7.4, N^+-$\underline{CH_2}$-CH), 5.59 (2H, m, CH-$\underline{CH_2}$), 5.88 (1H, m, $\underline{CH}$-CH_2) ^{13}C NMR (400 MHz, D_2O): δ_C 44.15, 51.92, 66.48, 123.61, 129.00.

Synthesis of CEM-DABCO: CEM-DABCO was synthesised using modifications to a literature reaction[29]. DABCO (1.222 g, 10.92 mmol) was dissolved in 20 mL of ethyl acetate, before ethyl chloroacetate (1.167 mL, 10.90 mmol) was added dropwise to the stirred solution and the reaction was left for 1 hour. The resulting white precipitate was washed with ethyl acetate (3x30 mL) and dried under vacuum to give CEM-DABCO as a white solid (1.9 g, 74%). ^1H NMR (400 MHz, D_2O): δ_H 1.20 (3H, t, $^3J_{HH}$ =7.2, $COOCH_2\underline{CH_3}$), 3.16 (6H, t, $^3J_{HH}$ =7.6, $(CH_2)_3N^+$), 3.59 (6H, t, $^3J_{HH}$ =7.6, $(CH_2)_3N$), 4.17 (2H, s, $N^+\underline{CH_2}COOEt$), 4.21 (2H, q, $^3J_{HH}$ =7.2, $COO\underline{CH_2}CH_3$). ^{13}C NMR (400 MHz, D_2O): 13.10, 43.97, 52.79, 61.67, 63.42, 164.70.

Synthesis of CM-DABCO: CEM-DABCO (13.94 g, 59.36 mmol) was dissolved in 20 ml water, before 1 M NaOH was added slowly. Following each addition, the pH was allowed to stabilise, before further addition, until 59.36 mmol of NaOH had been reacted, and the pH remained alkaline. The resulting solution was concentrated by rotary evaporation and freeze-dried, forming CM-DABCO as a white solid (12.9 g, 95.4%). ^1H NMR (400 MHz, D_2O): δ_H 3.13 (6H, t, $^3J_{HH}$ = 8.0, $(CH_2)_3N^+$), 3.56 (6H, t, $^3J_{HH}$ = 8.0, $(CH_2)_3N$), 3.75 (2H, s, $N^+\underline{CH_2}COO^-$) ^{13}C NMR (400 MHz, D_2O): δ_C 44.12, 52.24, 64.15, 168.74.

Synthesis of EA-DABCO: EA-DABCO was synthesised using modifications to a literature reaction[26]. DABCO (4.85 g, 43.25 mmol) was dissolved in 30 mL of ethyl

acetate, before 2-chloroethanol (0.58 mL, 8.65 mmol) was added dropwise to the stirred solution and the reaction was left for 48 hours. The resulting white precipitate was washed with ethyl acetate (3x30 mL) and dried under vacuum to give EA-DABCO as a white solid (0.57 g, 17%). ^{1}H NMR (400 MHz, D_2O): δ_H 3.11 (6H, t, $^{3}J_{HH}$ = 8.0, $(CH_2)_3N^+$), 3.36 (2H, t, $^{3}J_{HH}$ = 5.1, $N^+\underline{CH_2}CH_2$), 3.42 (6H, t, $^{3}J_{HH}$ = 8.0, $(CH_2)_3N$), 3.97 (2H, m). ^{13}C NMR (400 MHz, D_2O): δ_C 44.13, 52.95, 54.52, 65.71.

8.3 Catalyst pKa Measurements

The pKa of catalysts were measured using pH titration. To a starting 30 mM solution of catalyst, 2.5 M HCl was titrated in until a pH of 3.00 was reached. 2.5 M NaOH solutions were then titrated in, with the pH monitored using a pH meter with electrode. The pH of each catalyst was increased to at least 12.00, with amounts of NaOH needed recorded, and compared to a blank titration of water. Half-equivalences of the catalysts were then found from these, from which the pKa values were found. Titration curves obtained can be seen in Appendix 6.

8.4 Kinetic Studies

Kinetic studies were performed using a double mixing Bio-Logic SFM-3000 stopped flow mixer, coupled with an ASPEN TIDAS diode array spectrophotometer. Data was processed using Bio-Kine software from Bio-Logic. A cuvette of optical path length 0.75 mm was used in all experiments, and the mixing in all cases was 1:1:1 between the chemical components. All kinetic experiments were performed in triplets, with three triplets performed for each experiment not using delay times, with the average of each triplet used in analysis. In studies of catalyst stability using delay times, one triplet data set was run and analysed due to time restrictions.

An integration time of 1 ms was used in all experiments, with wavelengths between 181 and 731 nm measured for twenty seconds of reaction. Reactions were studied and observed via the analysis of spectra produced, with reaction time, wavelength, absorbance and delay time as the relevant tested variables in a single experiment. All experiments were performed at room temperature and pressure.

The final concentrations after mixing of 2 mM of organic substrate, 2 mM HOCl and 50 μM of catalyst were used in all experiments. Both the organic substrate and catalyst were within relevant buffer solutions. For the case where no catalyst was utilised, blank buffer was used instead.

Following extraction of data, the maximum increase of the gradient within the first 2 seconds of reaction at the desired wavelength was collected. From this, the catalytic factor was found, which compares the gradients with and without catalyst, in order to obtain a comparable value between different organic substrates and pH values. The equation to calculate the catalytic factor is shown in Equation 8.

$$Catalytic\ Factor = \frac{Maximum\ Rate\ with\ Catalyst}{Maximum\ Rate\ without\ Catalyst} (8)$$

For the experiments to study catalyst stability, delay times were utilised. After initial mixing of HOCl and catalyst solution, different delay times were initiated, before the addition of organic substrate. The difference between the maximum gradients of increase were then followed to observe possible catalyst degradation. Parameters were otherwise unchanged from experiments not using delay times.

9 Conclusions

The aim of the present work was to investigate the activity and stability of a selection of tertiary amine catalysts, in the reaction between hypochlorous acid and organic substrates. The impact of small changes to the catalyst structure was aiming to be investigated, in order to work towards finding the most suitable catalyst for various end-uses, particularly within catalytic bleaching of wood pulp.

Within literature, the studies of HOCl reactions with a variety of substrates could be found, including the effect of various conditions such as pH, substrate structure and component ratios. It was evident that whilst the phenomena of tertiary amines catalysing these reactions is known, the effect of changing the structure of the catalysts on their activities and stabilities had only been studied in a small number of cases.

Derivatives of the already industrially utilised DABCO were selected in order to observe this, due to DABCO, and its derivative CM-DABCO, already showing efficient bleaching outcomes in H_{cat} studies. Wood pulp bleaching is also the currently most researched area within the use of tertiary amine catalysts. Structures were selected based on ease of synthesis, as well as to obtain a range of derivative groups to understand the effect that these have.

Whilst the synthesis of many of the desired catalysts was performed successfully, EA-DABCO, featuring an 2-hydroxyethyl group, could only be produced in a low yield. It was seen that unlike what was expected, the structure of the derivative group only has a small impact on the pKa of the catalyst, with a change between 3.0 and 3.4 observed. In all cases then the pKa was similar to that of the second amine of DABCO itself (2.97).

Within kinetic studies, pH values of 3, 5 and 7 were tested with the organic substrates salicylic acid, 3-furoic acid and syringol. It was found that both pH and substrate structure play a role in the catalytic factors produced.

At pH 3, generally low catalytic factors could be observed, but these are increased with the nucleophilicity of the organic substrate, due to increased amounts of the reaction coming from HOCl compared to Cl_2 and Cl_2O. The highest catalytic factors were

found at pH 5, particularly for salicylic acid, and the difference caused by changes to the catalyst derivative group were the most evident. Between all the substrates, a similar order of catalyst activities was found, with CM-DABCO the most active and AA-DABCO the least. These activities fit well to the measured pKa values of the catalyst, with an increased catalytic factor coming from a pKa closer to the experimental pH of 5. pH 7 produced low catalytic factors for all the DABCO-derivatives due to the difference between this pH and the catalyst pKa values.

It can then be said that to improve the catalysts within H_{cat} pulp bleaching, a development should be done on the increasing of the catalyst pKa, with the benefit likely to increase even further as experimental pH is approached. Alternatively, it is possible using a lowered pH would also increase the effect of the catalyst used.

Considering then the catalyst stabilities, studies featuring delay times before substrate addition displayed that whilst DABCO undergoes first-order degradation, all the derivative structures are fully stable, up to at least 10 seconds of incubation with HOCl. Hence stability is not likely a problem when selecting and designing a DABCO-based catalyst.

Catalytic abilities are however likely to be very dependent on the reaction. In the case of syringol for example, where many reactions occur during the oxidation, some are catalyzed more efficiently than others, and this information cannot easily be read from the produced UV-spectra, especially when some result in chromophore degradation. Additionally, there may be inorganic reactions that are catalysed at a very different rate to organic ones, such as the reformation of ClO_2 in D_{cat} bleaching stages. Hence the results of this thesis do not give a full overview of the effect of the changed catalyst structures on their activities, and further testing of other reactions and catalyst structures is necessary.

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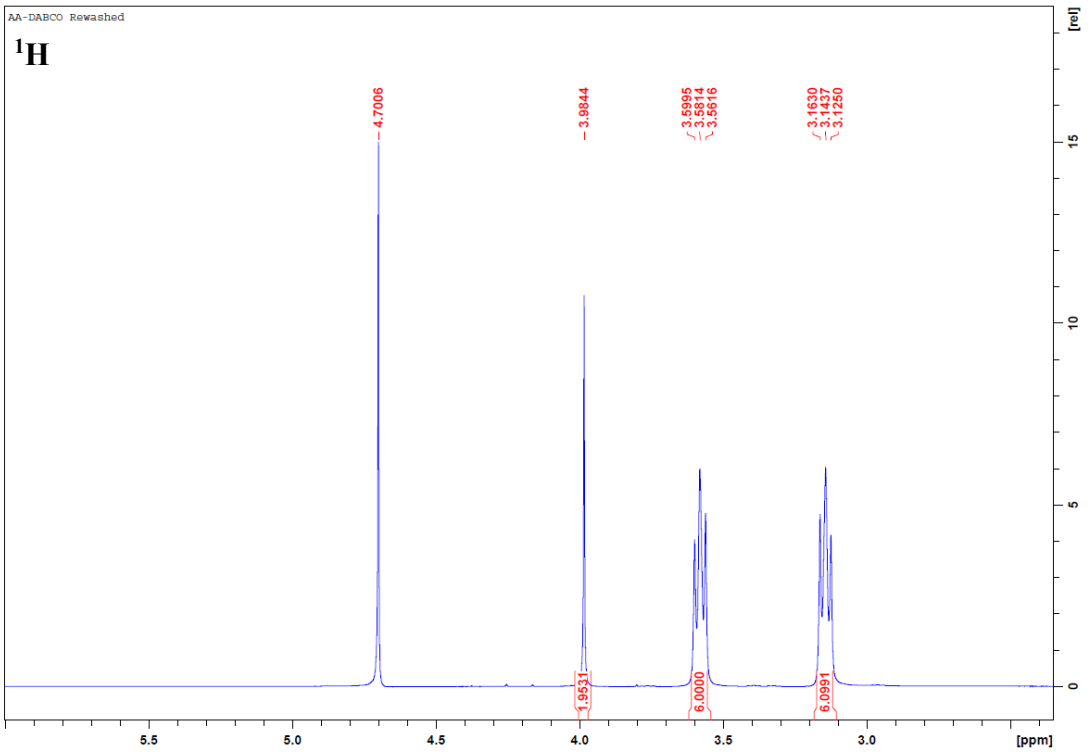
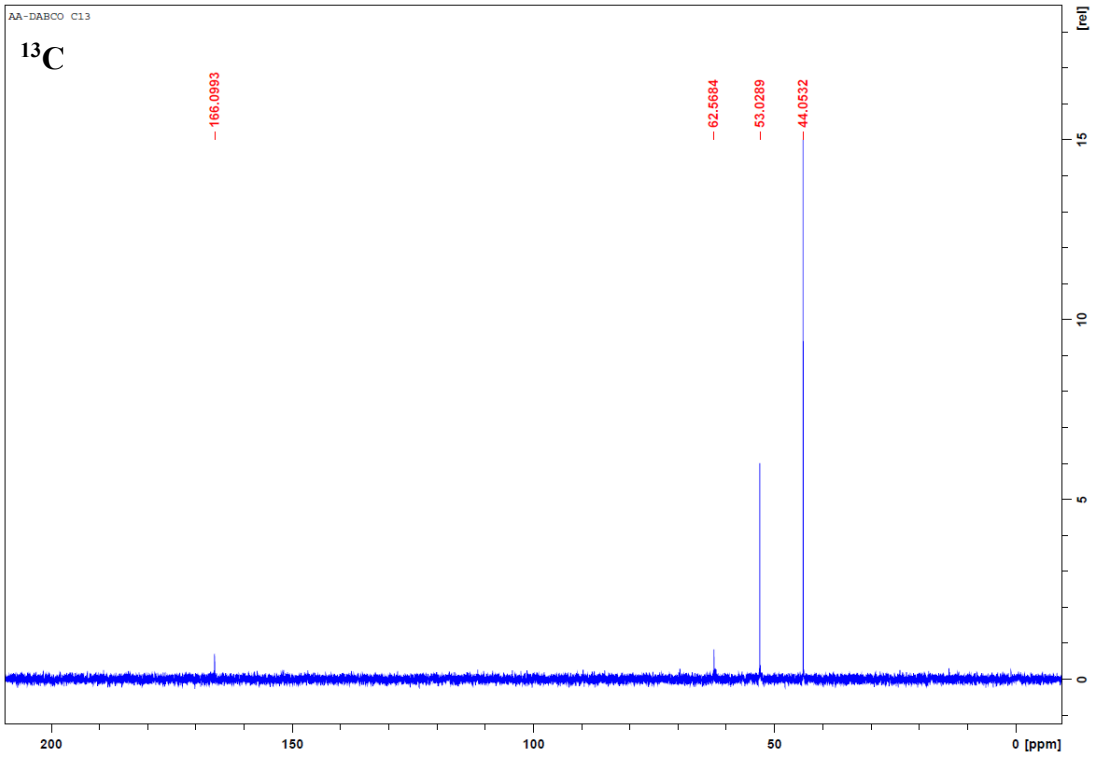
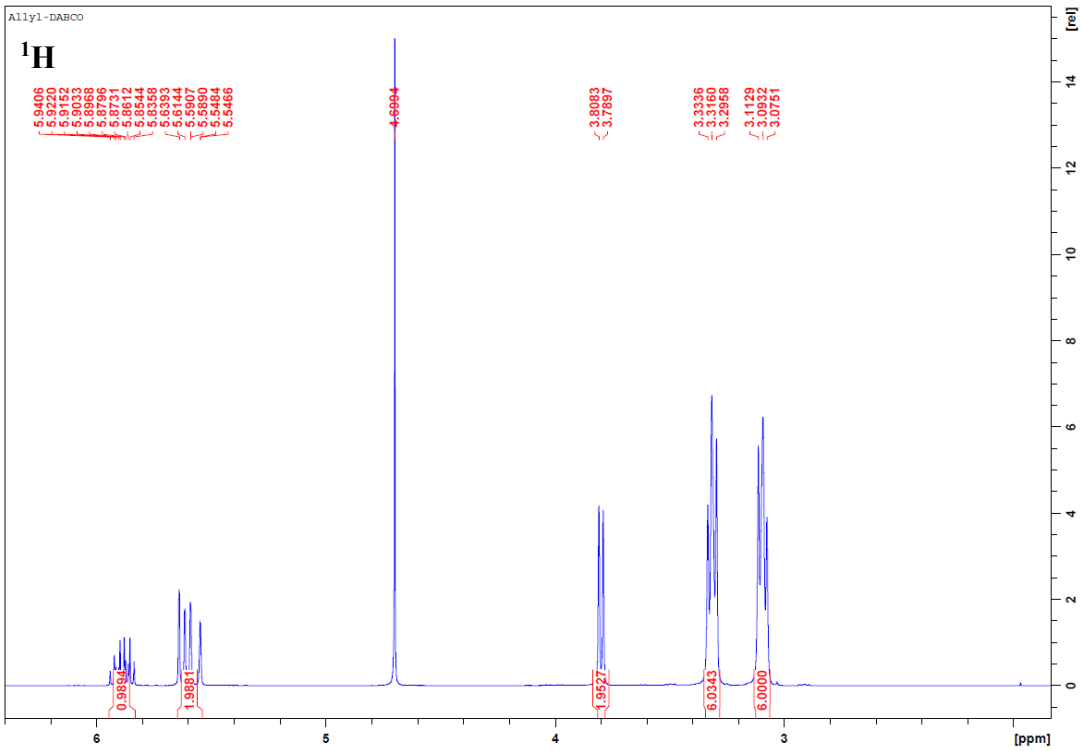
Appendices

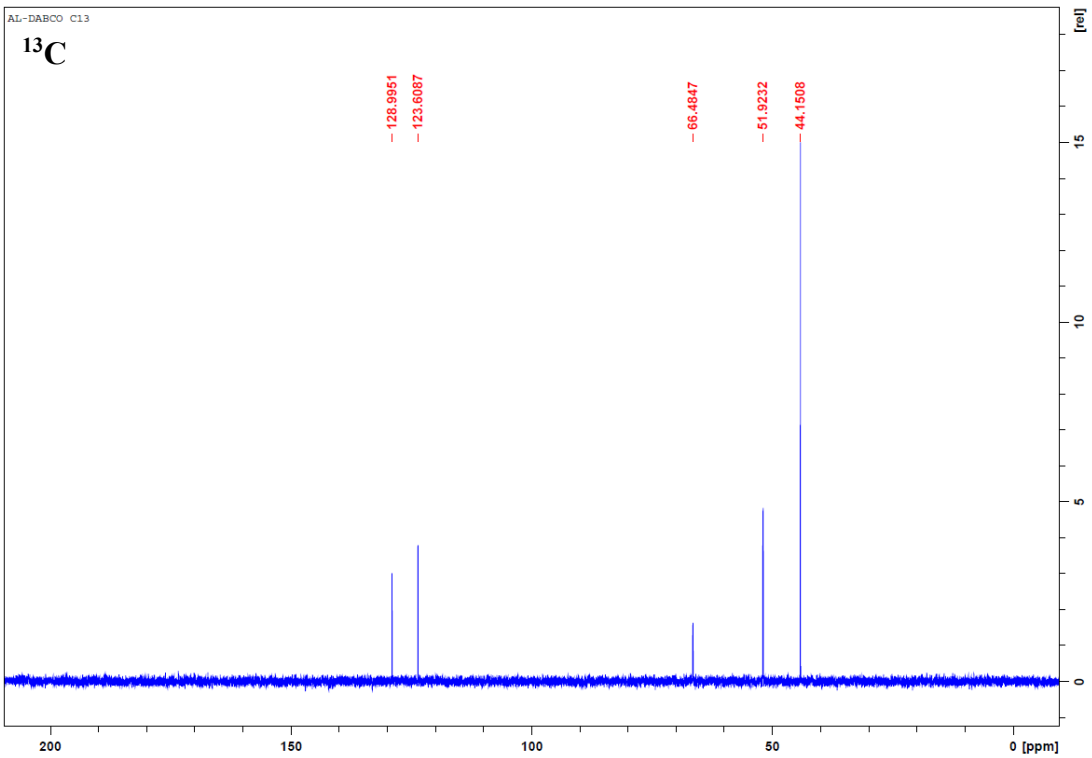
Appendix 1 – ^{1}H and ^{13}C NMR of AA-DABCO



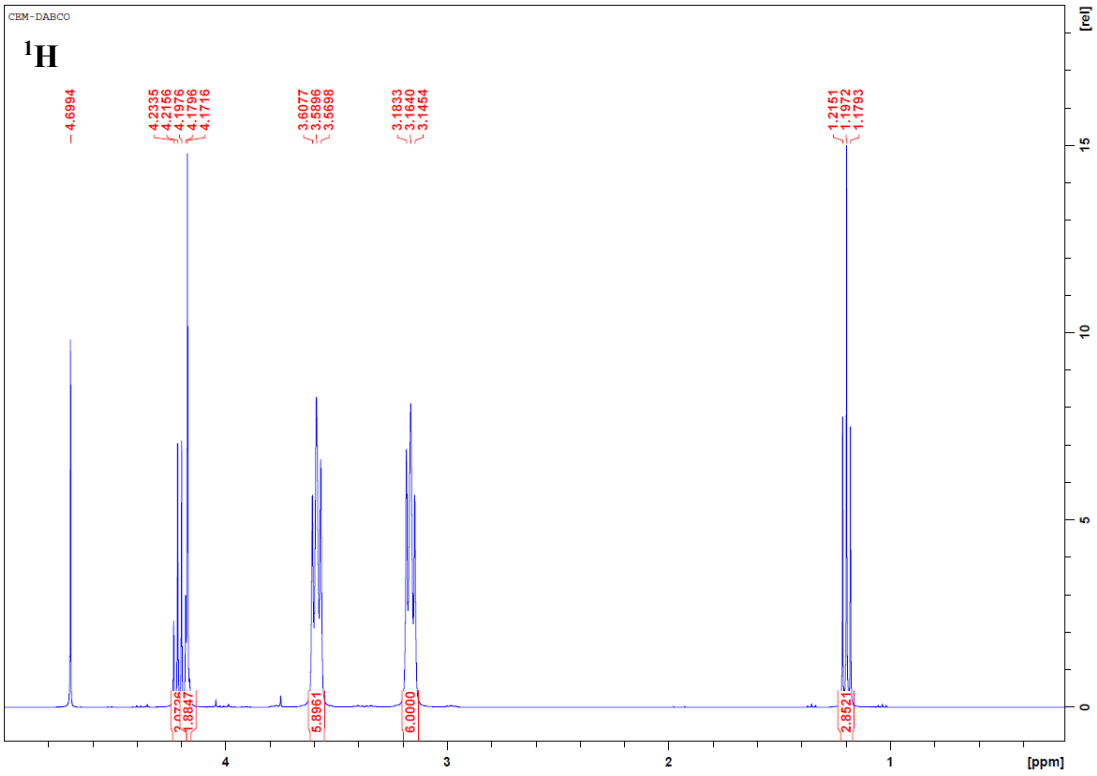


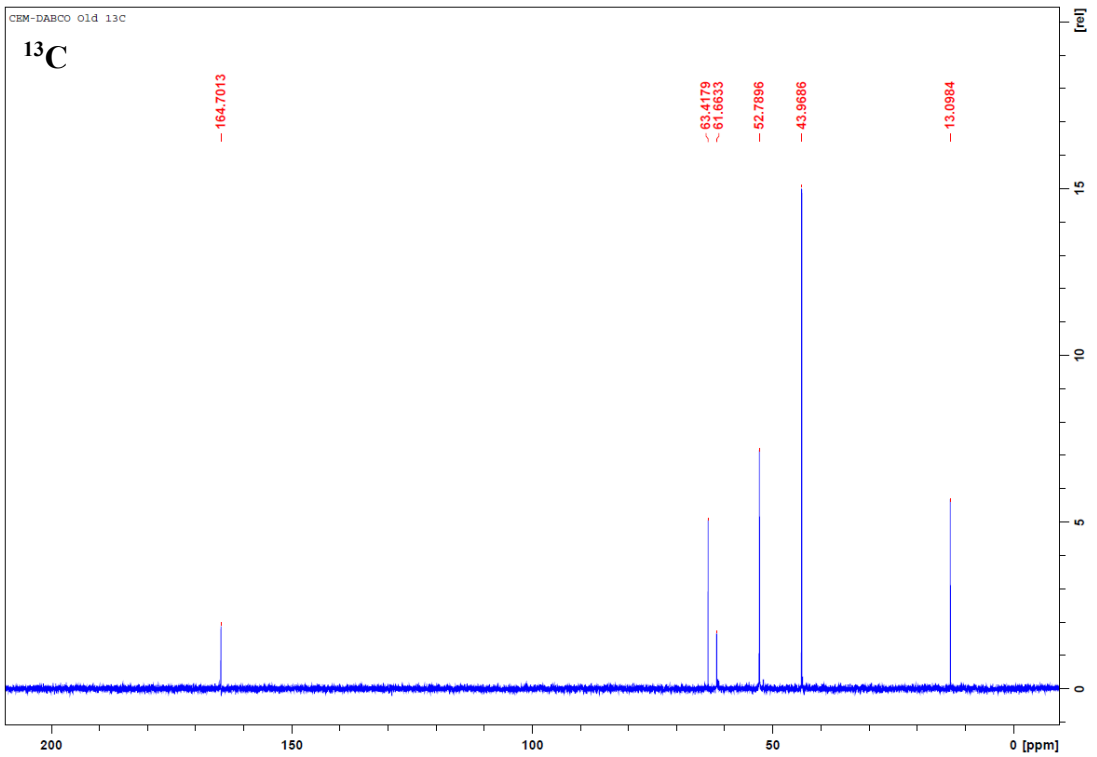
Appendix 2 – ^{1}H and ^{13}C NMR of AL-DABCO



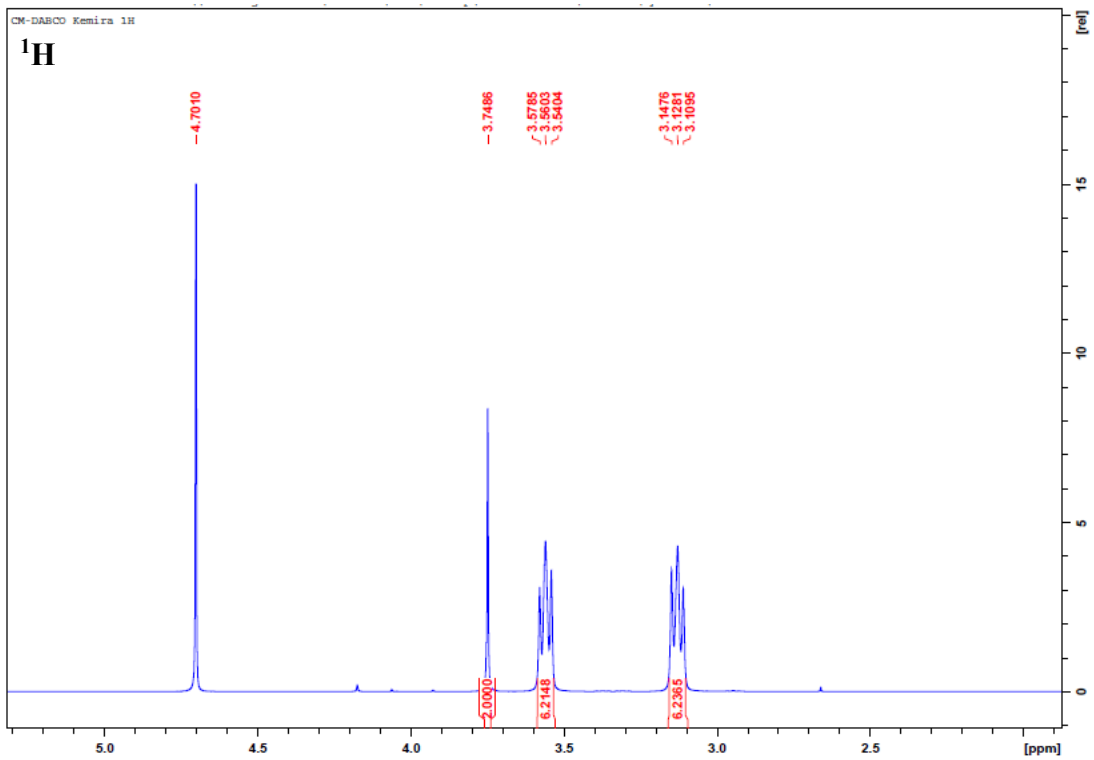


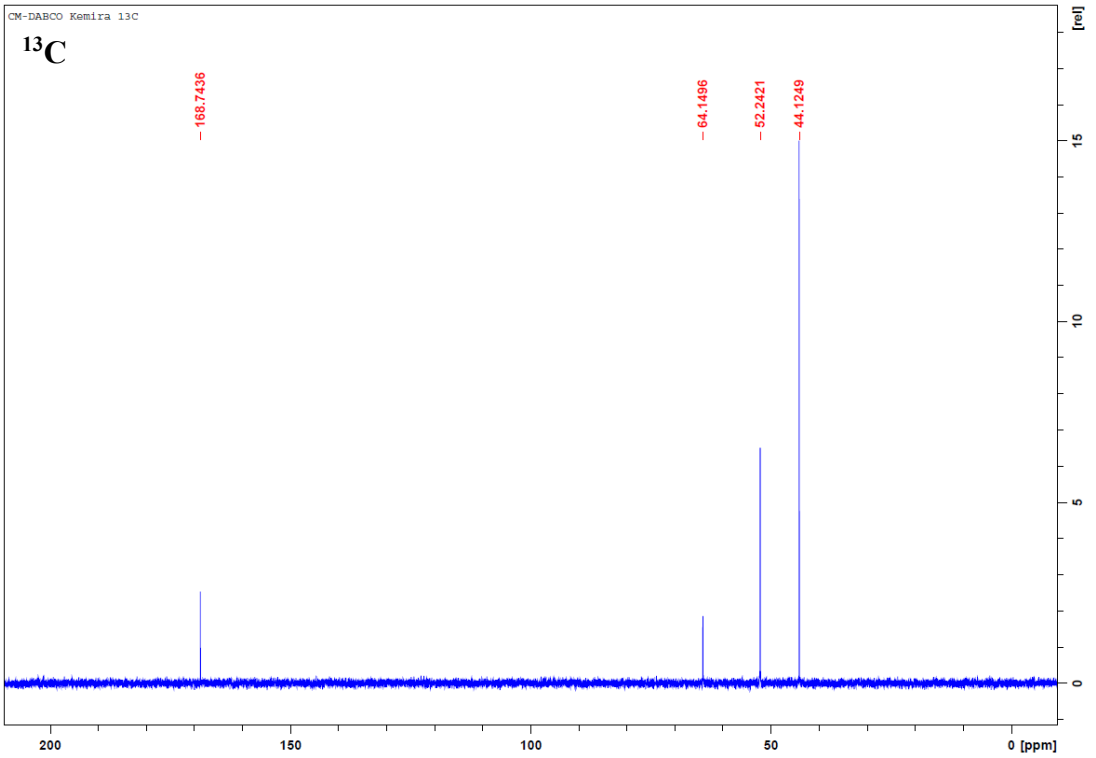
Appendix 3 – ^{1}H and ^{13}C NMR of CEM-DABCO



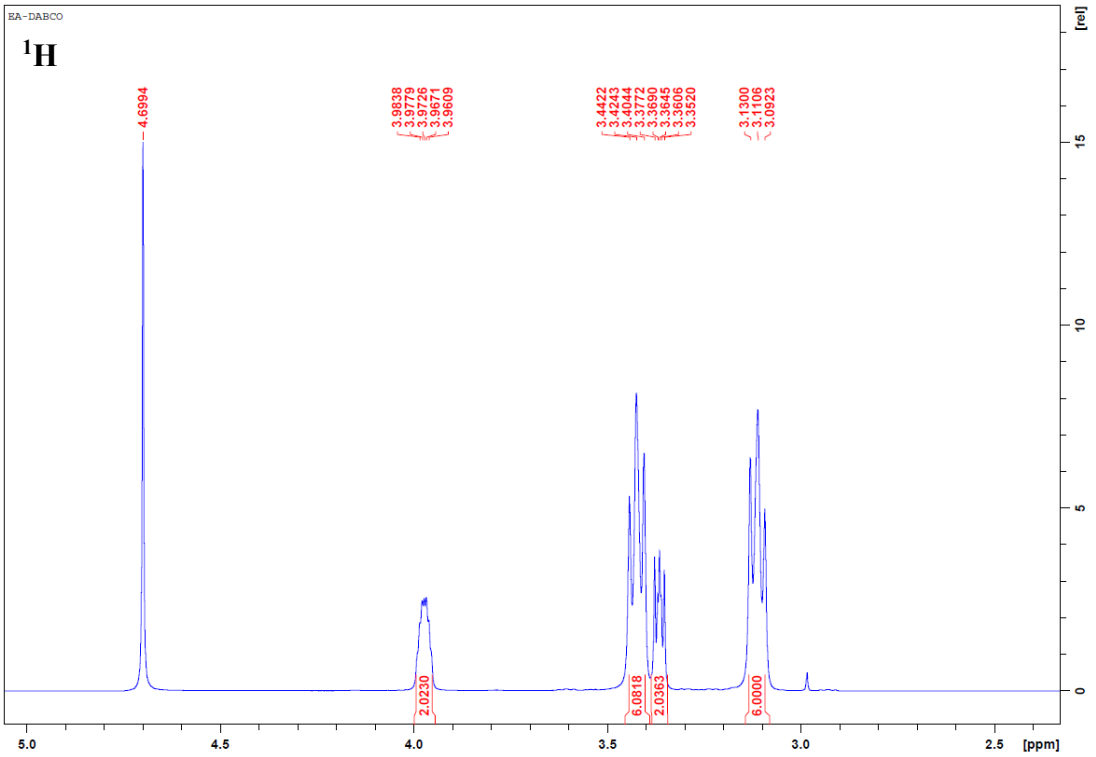


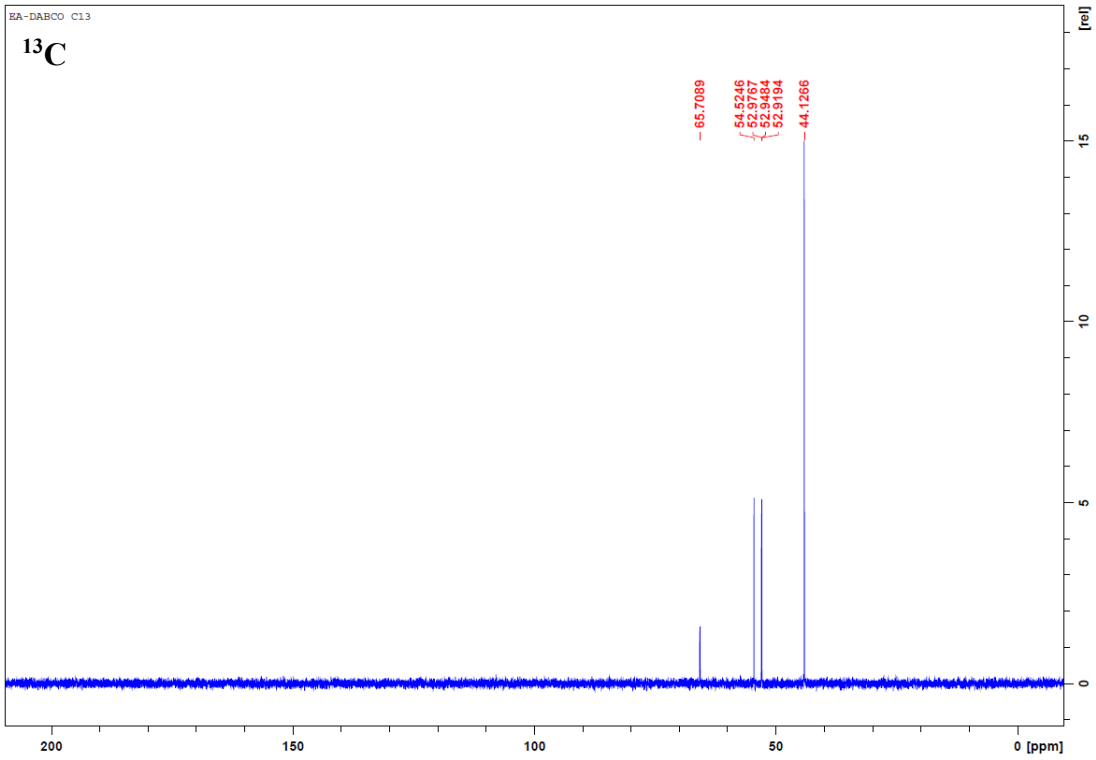
Appendix 4 – ^{1}H and ^{13}C NMR of CM-DABCO



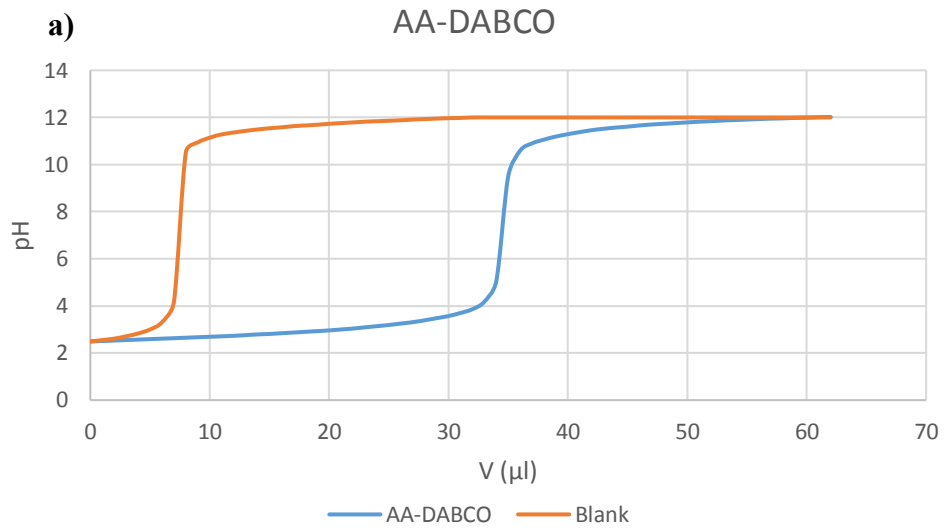


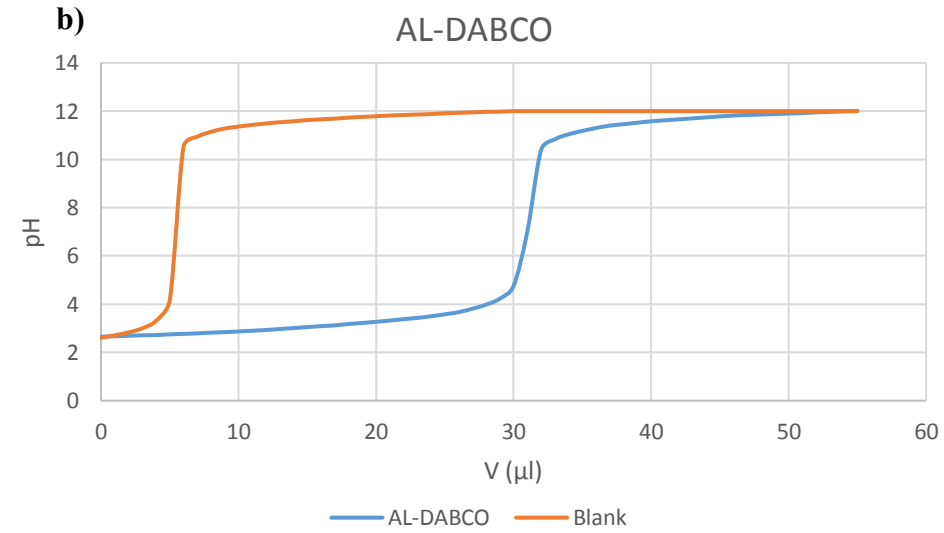
Appendix 5 – ^{1}H and ^{13}C NMR of EA-DABCO

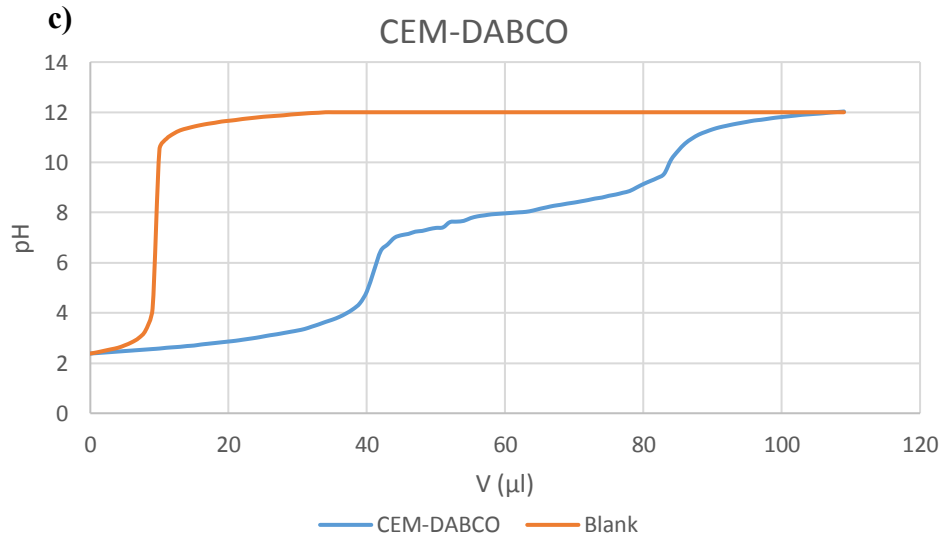




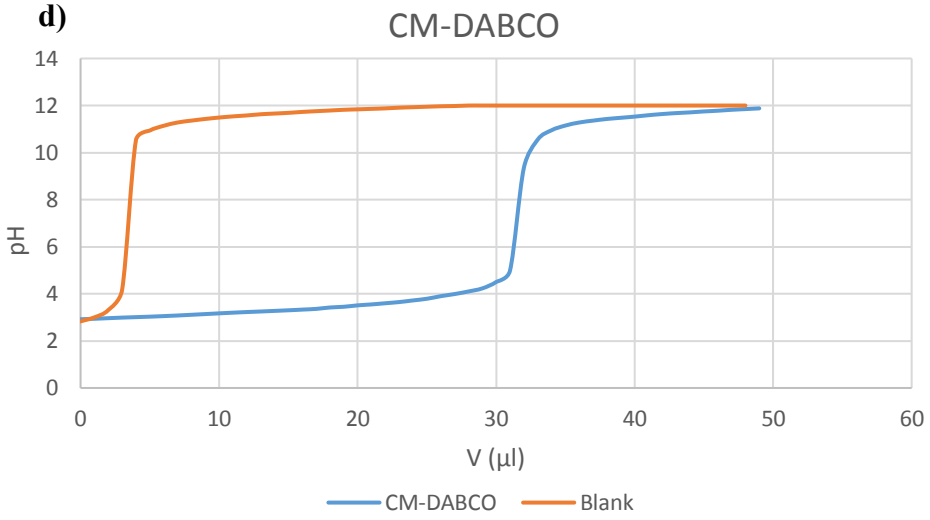
Appendix 6 – Catalyst pKa Titration Curves



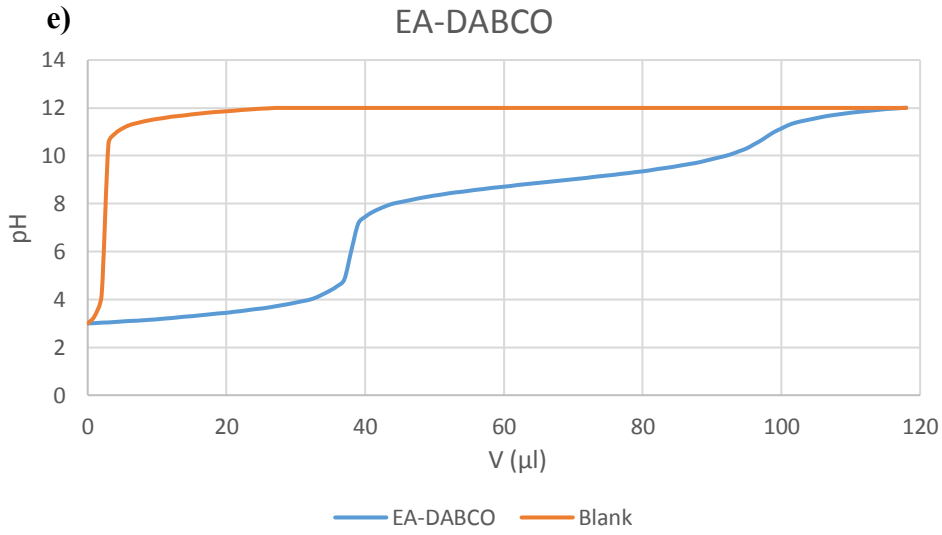




d)


CM-DABCO
14
12
10
8
6
4
2
0
pH
0
10
20
30
40
50
60
V (µl)
CM-DABCO
Blank

e)


EA-DABCO
14
12
10
8
6
4
2
0
pH
0
20
40
60
80
100
120
V (µl)
EA-DABCO
Blank

Appendix 7 – Catalytic Factors at pH 3, 5 and 7

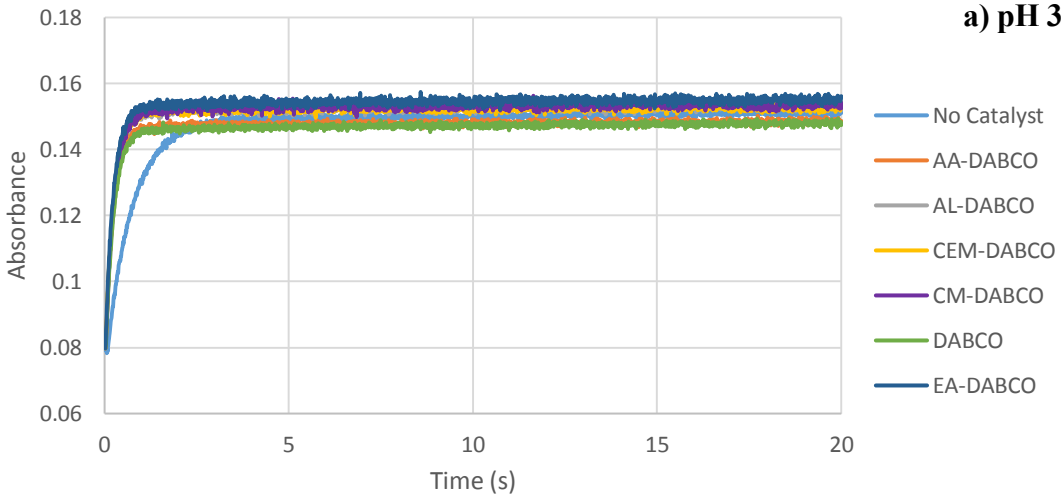
a) pH 3			Catalytic Factor					
Catalyst	**pKa**	**Order‡**	**Salicylic Acid**	**Order**	**3-Fuoric Acid**	**Order**	**Syringol**	**Order**
AA-DABCO	3.0	1	2.48 ± 0.07	4	3.69 ± 0.08	4	1.61 ± 0.01	1
AL-DABCO	3.2	3	2.62 ± 0.08	2	3.86 ± 0.09	3	1.45 ± 0.02	4
CEM-DABCO	3.1	2	2.59 ± 0.09	3	3.44 ± 0.08	5	1.54 ± 0.01	2
CM-DABCO	3.4	4	2.44 ± 0.08	5	4.22 ± 0.09	1	1.34 ± 0.01	5
EA-DABCO	3.4	4	2.71 ± 0.08	1	4.21 ± 0.10	2	1.47 ± 0.02	3
‡ Order from the lowest pKa to the highest.								

b) pH 5			Catalytic Factor					
Catalyst	**pKa**	**Order‡**	**Salicylic Acid**	**Order‡**	**3-Fuoric Acid**	**Order‡**	**Syringol**	**Order‡**
CM-DABCO	3.4	5	14.30 ± 0.86	1	5.24 ± 0.90	1	2.35 ± 0.04	1
EA-DABCO	3.4	3	11.17 ± 0.67	2	3.83 ± 0.66	2	2.26 ± 0.04	2
AL-DABCO	3.2	4	10.08 ± 0.60	3	3.10 ± 0.53	3	2.02 ± 0.03	4
CEM-DABCO	3.1	1	9.69 ± 0.58	4	2.87 ± 0.50	4	2.15 ± 0.04	3
AA-DABCO	3.0	1	9.29 ± 0.56	5	2.76 ± 0.48	5	1.92 ± 0.03	5
‡ Order from the highest pKa to the lowest.								

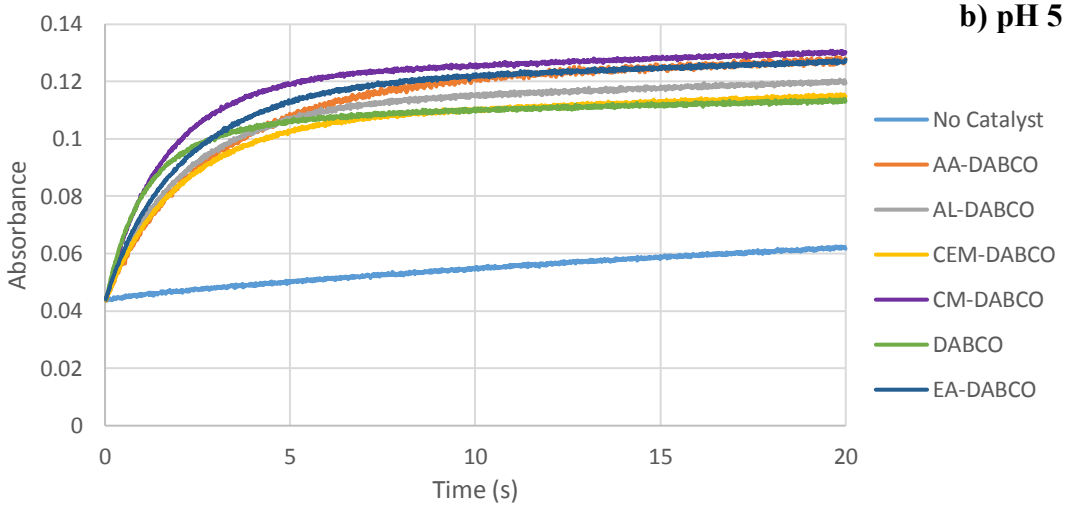
c) pH 7			Catalytic Factor					
Catalyst	**pKa**	**Order‡**	**Salicylic Acid**	**Order‡**	**3-Fuoric Acid**	**Order‡**	**Syringol**	**Order**
AA-DABCO	3.0	5	1.04 ± 0.04	4	1.01 ± 0.03	1	1.87 ± 0.06	5
AL-DABCO	3.2	3	0.93 ± 0.09	5	0.94 ± 0.05	5	2.04 ± 0.06	4
CEM-DABCO	3.1	4	1.07 ± 0.11	2	0.99 ± 0.02	3	2.61 ± 0.08	1
CM-DABCO	3.4	1	1.13 ± 0.10	1	1.00 ± 0.03	2	2.50 ± 0.07	2
EA-DABCO	3.4	1	1.07 ± 0.04	2	0.95 ± 0.03	4	2.20 ± 0.07	3
‡ Order from the highest pKa to the lowest.								

Appendix 8 – UV-Curves during Reaction – Salicylic Acid at 324 nm

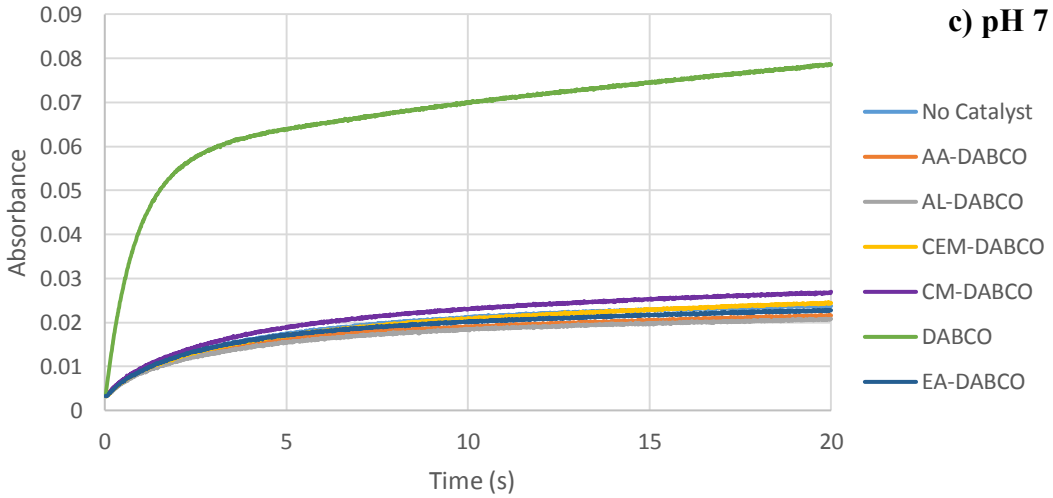
a) pH 3



b) pH 5

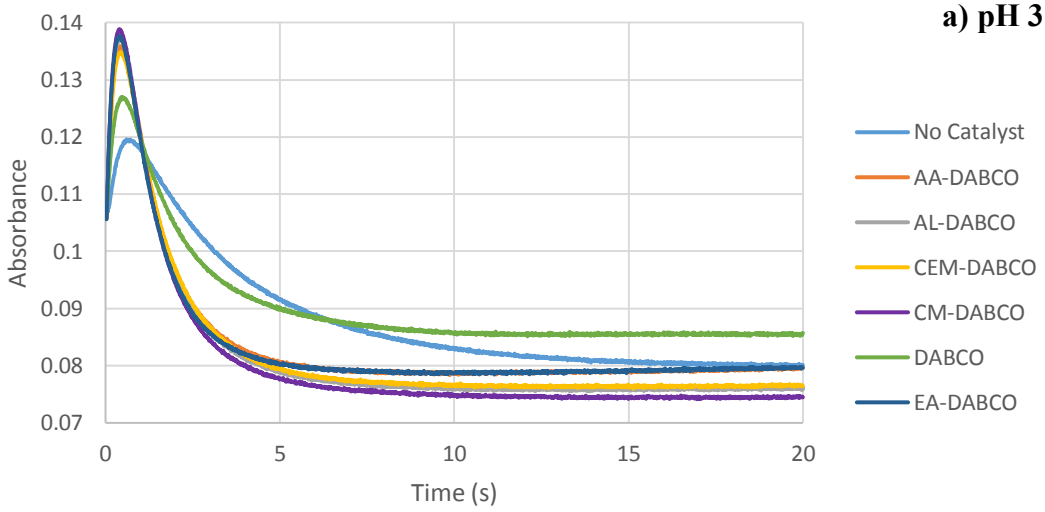


c) pH 7

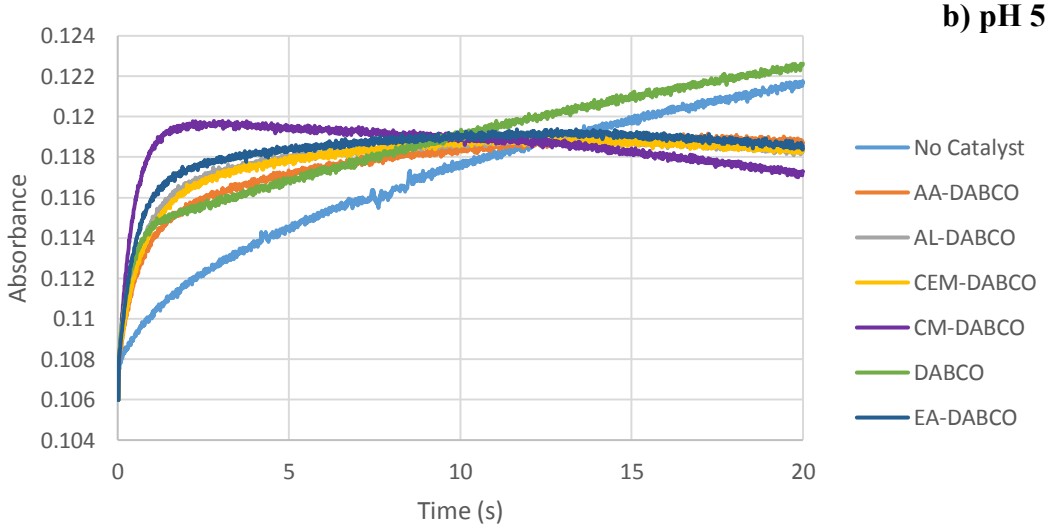


Appendix 9 – UV-Curves during Reaction – 3-Furoic Acid at 265 nm

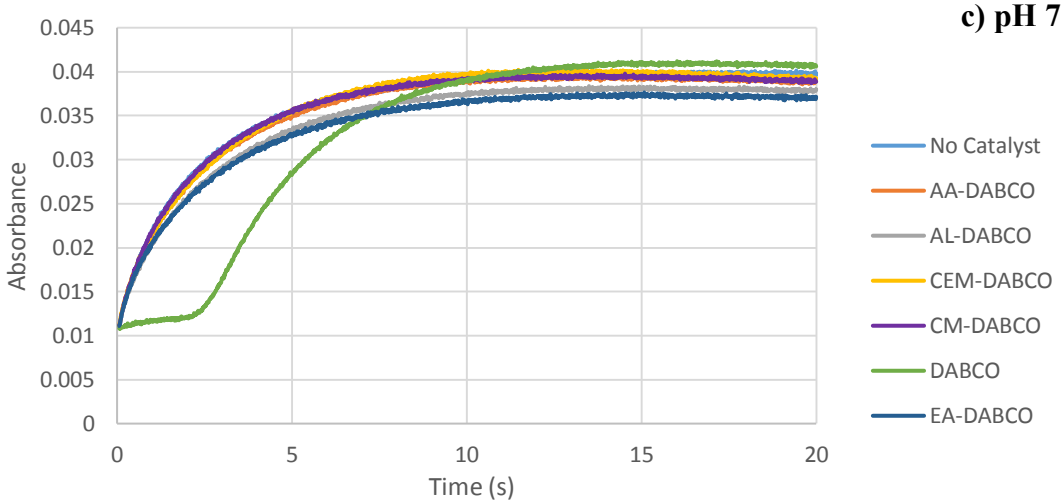
a) pH 3



b) pH 5

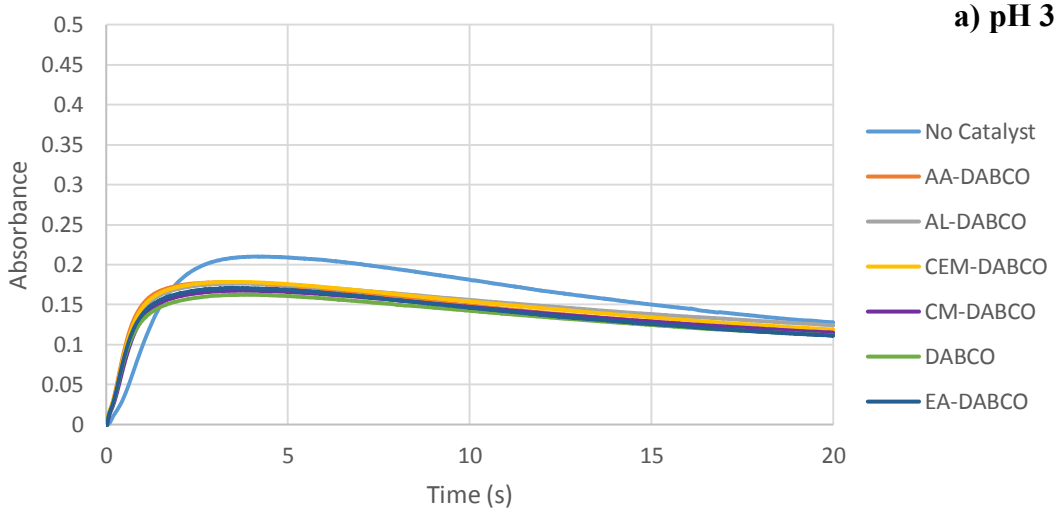


c) pH 7

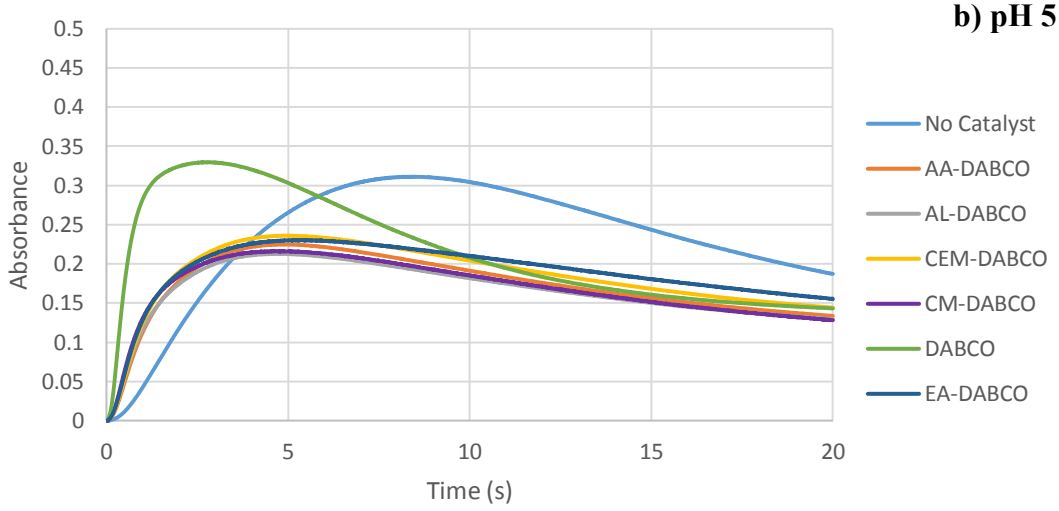


Appendix 10 – UV-Curves during Reaction – Syringol at 470 nm

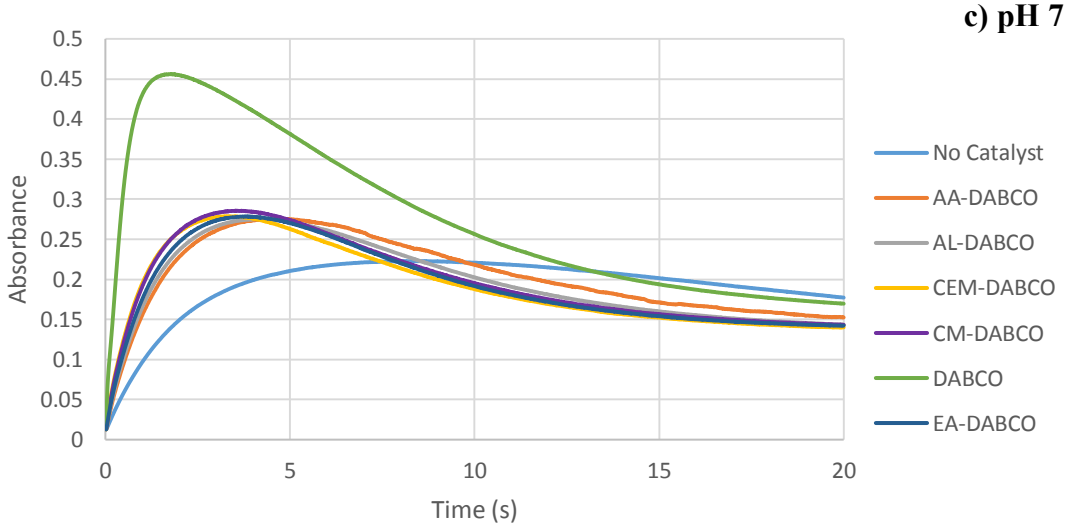
a) pH 3



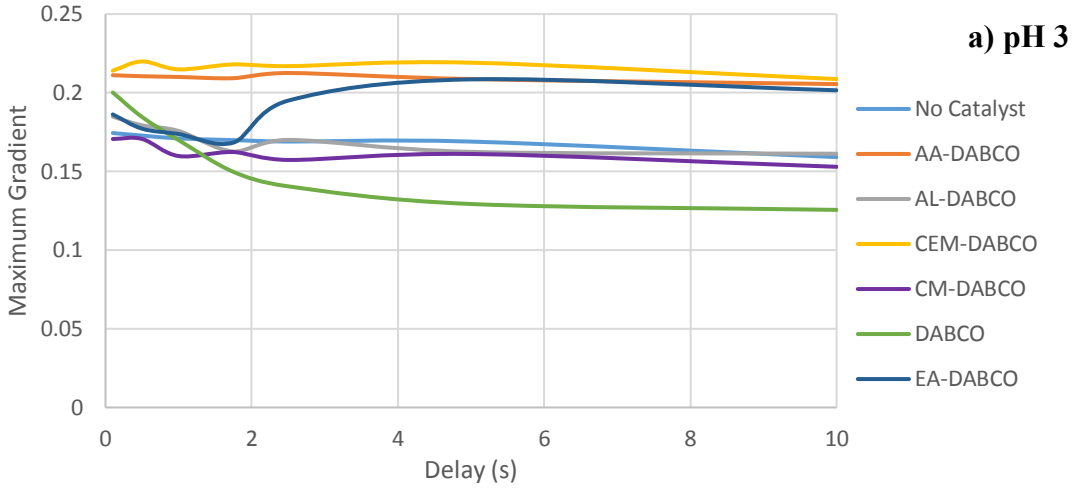
b) pH 5

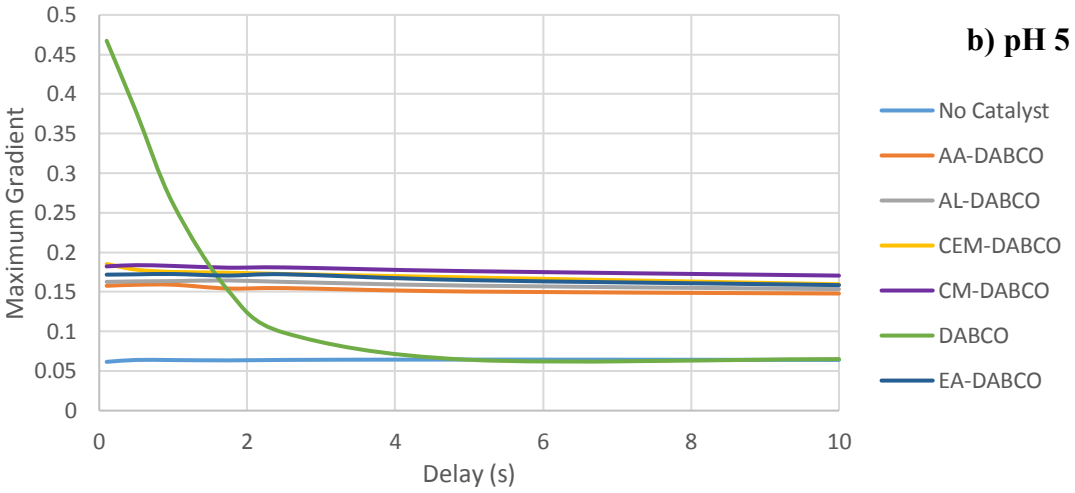


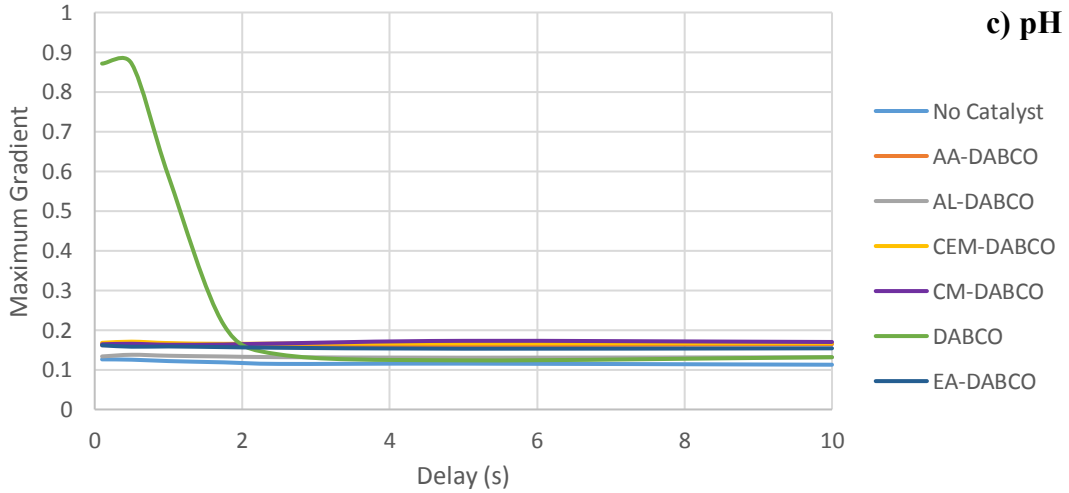
c) pH 7



Appendix 11 – Catalyst Stability Graphs - Syringol at pH 3, 5 and 7.







Appendix 12 – Catalyst Stability Tables – Gradient vs 0.1 s Delay

a) pH 3	Fraction vs 0.1 s					
Catalyst	**0.5 s**	**1 s**	**1.75 s**	**2.5 s**	**5 s**	**10 s**
None	0.99 ± 0.01	0.98 ± 0.02	0.97 ± 0.01	0.97 ± 0.02	0.97 ± 0.01	0.91 ± 0.02
DABCO	0.92 ± 0.02	0.85 ± 0.02	0.75 ± 0.02	0.70 ± 0.01	0.65 ± 0.02	0.63 ± 0.01
AA-DABCO	1.00 ± 0.01	0.99 ± 0.02	0.99 ± 0.01	1.01 ± 0.01	0.99 ± 0.01	0.97 ± 0.01
AL-DABCO	0.97 ± 0.03	0.95 ± 0.03	0.88 ± 0.04	0.92 ± 0.04	0.88 ± 0.04	0.87 ± 0.02
CEM-DABCO	1.03 ± 0.01	1.00 ± 0.02	1.02 ± 0.01	1.01 ± 0.02	1.02 ± 0.01	0.97 ± 0.02
CM-DABCO	1.00 ± 0.01	0.94 ± 0.01	0.95 ± 0.01	0.92 ± 0.03	0.94 ± 0.02	0.90 ± 0.02
EA-DABCO	0.95 ± 0.02	0.93 ± 0.02	0.90 ± 0.05	1.05 ± 0.08	1.12 ± 0.02	1.08 ± 0.02

b) pH 5	Fraction vs 0.1 s					
Catalyst	**0.5 s**	**1 s**	**1.75 s**	**2.5 s**	**5 s**	**10 s**
None	1.04 ± 0.03	1.04 ± 0.05	1.03 ± 0.03	1.04 ± 0.04	1.05 ± 0.03	1.04 ± 0.05
DABCO	0.81 ± 0.01	0.56 ± 0.01	0.32 ± 0.01	0.21 ± 0.01	0.14 ± 0.03	0.14 ± 0.02
AA-DABCO	1.01 ± 0.02	1.01 ± 0.02	0.98 ± 0.02	0.98 ± 0.02	0.95 ± 0.02	0.94 ± 0.02
AL-DABCO	1.00 ± 0.03	1.01 ± 0.04	1.01 ± 0.05	1.00 ± 0.04	0.97 ± 0.04	0.94 ± 0.03
CEM-DABCO	0.96 ± 0.01	0.95 ± 0.02	0.94 ± 0.01	0.93 ± 0.02	0.91 ± 0.01	0.86 ± 0.02
CM-DABCO	1.01 ± 0.01	1.00 ± 0.01	0.99 ± 0.01	0.99 ± 0.02	0.97 ± 0.02	0.94 ± 0.02
EA-DABCO	1.00 ± 0.02	1.00 ± 0.02	0.99 ± 0.05	1.00 ± 0.09	0.96 ± 0.02	0.92 ± 0.02

c) pH 7	Fraction vs 0.1 s					
Catalyst	**0.5 s**	**1 s**	**1.75 s**	**2.5 s**	**5 s**	**10 s**
None	0.99 ± 0.02	0.97 ± 0.03	0.94 ± 0.01	0.91 ± 0.02	0.91 ± 0.02	0.89 ± 0.03
DABCO	1.00 ± 0.01	0.67 ± 0.01	0.24 ± 0.01	0.16 ± 0.01	0.14 ± 0.02	0.15 ± 0.01
AA-DABCO	1.01 ± 0.02	1.02 ± 0.02	0.99 ± 0.02	1.01 ± 0.02	1.00 ± 0.02	1.02 ± 0.02
AL-DABCO	1.03 ± 0.04	1.01 ± 0.04	1.00 ± 0.06	0.99 ± 0.05	0.98 ± 0.05	0.99 ± 0.04
CEM-DABCO	1.02 ± 0.02	1.00 ± 0.02	0.99 ± 0.02	0.99 ± 0.02	0.99 ± 0.01	1.00 ± 0.02
CM-DABCO	1.01 ± 0.01	0.99 ± 0.01	1.00 ± 0.01	1.01 ± 0.03	1.05 ± 0.02	1.04 ± 0.02
EA-DABCO	0.98 ± 0.02	0.98 ± 0.02	0.97 ± 0.05	0.96 ± 0.1	0.95 ± 0.02	0.95 ± 0.03